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Proceedings of The Second Pan American Scientific Congress

WASHINGTON, U. S. A.

Monday, December 27, 1915
to Saturday, January 8, 1916

Compiled and edited under the direction of
Glen Levin Swiggett, Assistant Secretary General

SECTION VIII

(IN TWO PARTS)

PART 2

PUBLIC HEALTH AND MEDICINE

WILLIAM C. GORGAS, SURGEON GENERAL U. S. A., CHAIRMAN

VOL. X

WASHINGTON
GOVERNMENT PRINTING OFFICE
1917

214673
DEC 13 1917
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Letters of Transmittal.

WASHINGTON, D. C., *May 31, 1917.*

SIR: Pursuant to the recommendation of the executive committee of the Second Pan American Scientific Congress, which was held in Washington December 27, 1915–January 8, 1916, and by the cooperation of the United States Congress (urgent deficiency bill, Sept. 8, 1916), the papers and discussions of that great international scientific gathering have been compiled and edited for publication under the able direction of the Assistant Secretary General, Dr. Glen Levin Swiggett. In this volume is contained the report of Section VIII, of which Gen. W. C. Gorgas, of the executive committee, was chairman.

In my formal report, which has already been submitted, I enlarged upon the importance of the Second Pan American Scientific Congress, its large attendance, and the high quality of its papers and discussions. I will, therefore, in this letter, which, in slightly varied form, introduces each volume, make only a few general references.

All of the 21 Republics of the Western Hemisphere were represented by official delegates at the Congress. Unofficial delegates, moreover, from the leading scientific associations and educational institutions of these Republics presented papers and took part in its deliberations. The papers and discussions may be considered, therefore, as an expression of comprehensive Pan American scientific effort and possess, in consequence, inestimable value.

The Congress was divided into nine main sections, which, with their chairmen, were as follows:

I. ANTHROPOLOGY. W. H. Holmes.
II. ASTRONOMY, METEOROLOGY, AND SEISMOLOGY. Robert S. Woodward.
III. CONSERVATION OF NATURAL RESOURCES, Agriculture, Irrigation, and Forestry. George M. Rommel.
IV. EDUCATION. P. P. Claxton.
V. ENGINEERING. W. H. Bixby.
VI. INTERNATIONAL LAW, PUBLIC LAW, AND JURISPRUDENCE. James Brown Scott.
VII. MINING, METALLURGY, ECONOMIC GEOLOGY, AND APPLIED CHEMISTRY. Hennen Jennings.
VIII. PUBLIC HEALTH AND MEDICAL SCIENCE. William C. Gorgas.
IX. TRANSPORTATION, COMMERCE, FINANCE, AND TAXATION. L. S. Rowe.

These sections, in turn, were further subdivided into 45 subsections.

Over 200 delegates were in attendance from the Latin American Republics, while over a thousand from the United States participated in its meetings. The discussions and proceedings of the Congress attracted world-wide attention, and it was undoubtedly the greatest international scientific meeting that has assembled anywhere in the history of the Western Hemisphere and possibly of the world. It was, therefore, a fitting successor to the first Pan American Scientific Congress, which assembled in Santiago, the capital of Chile, in 1908, and to its predecessors, confined to Latin American representation, which in former years met, respectively, in Rio de Janeiro, Montevideo, and Buenos Aires. Its success was a logical result of these preceding gatherings in Latin America and of the hearty cooperation of the Latin American Governments and scientists.

To those who may have their attention brought only to the individual volumes covering the papers and discussions and who wish to know more of the proceedings of the Congress and the results accomplished by it, it is recommended that they should

also read "The Final Act—An Interpretative Commentary Thereon," prepared under the direction of Dr. James Brown Scott, reporter general of the Congress, and the report of the secretary general, prepared by the latter and the assistant secretary general, Dr. Glen Levin Swiggett. In these will be found not only the final act and the illuminating comment thereon but lists of delegates, participating Governments, societies, educational institutions, and other organizations, together with a careful story and history of the Congress. They can be obtained by addressing the Director General of the Pan American Union, Washington, D. C.

In conclusion, I want to briefly repeat, as secretary general of the Congress, my appreciation, already expressed in my formal report, of the hearty cooperation in making the Congress a success given by everyone concerned from the President of the United States, yourself as Secretary of State, and the delegates of Latin America and the United States, down to the office employees. The great interest manifested by the permanent executive committee, headed by Mr. William Phillips, then Third Assistant Secretary of State, the Carnegie Endowment for International Peace through its secretary, Dr. James Brown Scott, and the executive aid of Dr. Glen Levin Swiggett, as assistant secretary general, were vitally instrumental in making the gathering memorable. The Pan American Union, the official international organization of all the American Republics, and whose governing board is made up of the Latin American diplomats in Washington and the Secretary of State of the United States, lent the favorable influence of that powerful organization to the success of the Congress and authorized me as the director general of the Union to also take up the duties of secretary general of the Congress.

Yours, very truly,

(Signed) JOHN BARRETT,
Secretary General.

The Honorable The SECRETARY OF STATE,
Washington, D. C.

WASHINGTON, D. C., *31 de maio de 1917.*

EXMO. SNR.: Em cumprimento de uma recommendação emanada da Commissão Executiva do Segundo Congresso Scientifico Pan Americano, que teve lugar em Washington, de 27 de dezembro de 1915 a 8 de janeiro de 1916, e, devido ao auxilio do Congresso dos Estados Unidos (Lei para Orçamentos extraordinarios de 8 de setembro, 1916) as memorias e as discussões dessa assembléa scientifica internacional, foram colligidas e preparadas para publicação sob a proficiente direcção do Secretario Geral Adjuncto, Dr. Glen Levin Swiggett. Este volume comprehende o relatorio da secção VIII que foi presidida pelo General W. C. Gorgas, da Commissão Executiva.

No meu relatorio official, que já tive a honra de apresentar, me detive sobre a importancia do Segundo Congresso Scientifico Pan Americano, da sua grande concorrencia e da alta importancia das theses e das discussões. Na presente nota, portanto, de uma maneira muito ligeira, destinada a apresentar cada um dos volumes, eu farei apenas algumas referencias muito geraes.

Todas as Republicas do Hemispherio Occidental, vinte e uma em numero, se achavam representadas por delegados officiaes ao Congresso. Delegados sem nomeação dos Governos, mas representando as mais notaveis sociedades scientificas e instituições de ensino dessas republicas apresentaram theses e tomaram parte nas deliberações. As memorias e discussões devem ser consideradas portanto, como a expressão de um justificavel trabalho scientifico Pan Americano e possue, por esse motivo, um valor sem egual.

O Congresso foi dividido em nove secções principaes, que a seguir enuméro, com os nomes dos seus presidentes:

I. ANTHROPOLOGIA. W. H. Holmes.

II. ASTRONOMIA, METEREOLOGIA E SISMOLOGIA. Robert S. Woodward.

III. Conservação da Riqueza Nacional, Agricultura, Irrigação e Silvicultura. George M. Rommel.
IV. Instrucção. P. P. Claxton.
V. Engenharia. W. H. Bixby.
VI. Direito Internacional, Direito Publico e Jurisprudencia. James Brown Scott.
VII. Minas, Metallurgia, Geologia Practica e Chimica Industrial. Hennen Jennings.
VIII. Saude Publica e Sciencias Medicas. William C. Gorgas.
IX. Vias de Communicação, Commercio, Finanças e Impostos. L. S. Rowe.

Estas secções, por seu lado, eram subdivididas em 45 subsecções.

Mais de 200 delegados das Republicas da America Latina frequentaram as sessões emquanto os Estados Unidos se achavam representados por mais de mil pessoas. As discussões e os relatorios do Congresso attrahiram a attenção de todo o mundo e foi sem duvida a maior assemblea scientifica que se realizou no Hemispherio Occidental e talvez em todo o mundo. Foi sem duvida um idoneo continuador do Primeiro Congresso Scientifico Pan-Americano, que se celebrou em Santiago, capital da Republica Chilena em 1908 e das anteriores assembleas que previamente se tinham realizado, apenas com delegados da America Latina e que se reuniram em annos anteriores no Rio de Janeiro, Montevideu e Buenos Aires. O seu successo foi um resultado logico das reuniões previas na America Latina e do cordial concurso dos Governos da America latina e dos seus homens de sciencia.

A aquelles que não quizerem limitar-se a consultar os volumes que contém as memorias e as discussões e que desejarem conhecer alguma cousa mais dos trabalhos do Congresso e dos resultados por elle alcançado se lhes recommenda a leitura da Acta Final—a exposição geral concernente á mesma—publicada sob a direcção do Sr. Dr. James Brown Scott, Relator Geral do Congresso, e o relatorio do Secretario Geral, preparado pelo abaixo assignado e pelo Secretario Geral Adjuncto Sr. Dr. Glen Levin Swiggett. Nestes trabalhos encontrar-se-hão não sómente a acta final mas tambem um magnifico commentario, a lista dos delegados dos Governos que adheriram, sociedades, instituições de ensino e outras corporações, seguidas de uma cuidadosa historia do Congresso. Estes volumes continuam á disposição dos que os pedirem ao Director Geral da União Pan-Americana, Washington, D. C.

Em conclusão, eu desejo repetir, em duas palavras, como Secretario Geral do Congresso, o meu apreço e reconhecimento, que já tive occasião de exprimir no meu relatorio official, pela cordial cooperação que por todos me foi prestada para levar a bom exito este congresso, desde o Presidente dos Estados Unidos, V. Exa., como Secretario d'Estado, os Senhores Delegados da America Latina e dos Estados Unidos até os diversos funccionarios do Congresso. O grande interesse manifestado pela Commissão Permanente Executiva presidida pelo Sr. William Phillips, ao tempo terceiro Sub-secretario d'Estado, pelo Instituto de Carnegie para a Paz Internacional na pessoa do Sr. Dr. James Brown Scott, assim como a collaboração prestada pela Sr. Dr. Glen Levin Swiggett, como Secretario Geral Adjuncto, constituiram obras basilares para o successo desta reunião.

A União Pan-Americana, instituição internacional sustentada por todas as Republicas Americanas e cujo Conselho de Administração é constituido pelos representantes diplomaticos em Washington e pelo Secretario d'Estado dos Estados Unidos, contribuiu com a sua poderosa influencia para o bom exito do Congresso e me auctorizou a servir de Secretario Geral do Congresso.

Com a maior consideração, subscrevo-me

De V. Exa.,
Vor. Mto. Atto.,
John Barrett,
Secretario Geral.

Exmo. Snr. Secretario de Estado,
Washington, D. C.

WASHINGTON, D. C., *31 de mayo de 1917.*

SEÑOR:

En cumplimiento de una recomendación emanada de la Comisión Ejecutiva del Segundo Congreso Científico Panamericano que se reunió en Wáshington desde el 27 de diciembre de 1915 hasta el 8 de enero de 1916 y gracias a la cooperación al efecto prestada por el Congreso de los Estados Unidos mediante su ley sobre rectificación del presupuesto dictada el 8 de setiembre de 1916, hánse recopilado y preparado para su publicación, bajo la hábil dirección del Sr. Dr. Glen Levin Swiggett, Subsecretario General, las memorias presentadas a dicho Congreso y los debates a que dieron lugar. El presente volumen contiene el informe relativo a la Sección VIII, de la cual fué presidente el General W. C. Gorgas, miembro de la Comisión Ejecutiva.

En el informe general que ya tuve el honor de presentarle, me fué dable considerar detenidamemte la importancia del Segundo Congreso Científico Panamericano, la numerosa concurrencia que al mismo asistió y el elevado mérito de las memorias presentadas y de los debates que en aquel se suscitaron. Por consiguiente, he de limitarme en la presente, destinada a servirle de mera introducción a cada uno de los volúmenes, a algunas consideraciones de carácter general.

En el Congreso estuvieron representadas por medio de delegaciones oficiales las veinte y una repúblicas del Hemisferio Occidental. También asistieron al mismo, tomando participación en sus debates y presentando trabajos personales, delegados particulares de los principales cuerpos científicos y de los institutos docentes de esas mismas repúblicas. En tal virtud, las memorias y los debates mencionados deben ser considerados como la expresión de un amplio esfuerzo científico panamericano, encerrando, por lo tanto, un valor inestimable.

El Congreso estuvo dividido en nueve secciones principales que en seguida paso a enumerar junto con el nombre de sus presidentes. Fueron las siguientes:

I. ANTROPOLOGÍA. W. H. Holmes.

II. ASTRONOMÍA, METEOROLOGÍA Y SISMOGRAFÍA. Robert S. Woodward.

III. CONSERVACIÓN DE LAS FUENTES NATURALES DE RIQUEZA, AGRICULTURA, IRRIGACIÉN Y SELVICULTURA. George M. Rommel.

IV. INSTRUCCIÓN. P. P. Claxton.

V. INGENIERÍA. W. H. Bixby.

VI. DERECHO INTERNACIONAL, DERECHO PÚBLICO Y JURISPRUDENCIA. James Brown Scott.

VII. MINERÍA, METALURGIA, GEOLOGÍA ECONÓMICA Y QUÍMICA APLICADA. Hennen Jennings.

VIII. SALUBRIDAD PÚBLICA Y CIENCIA MÉDICA. William C. Gorgas.

IX. TRASPORTE, COMERCIO, FINANZAS E IMPUESTOS. L. S. Rowe.

Estas secciones estuvieron divididas, a su vez, en cuarenta y cinco subsecciones.

De las repúblicas latino-americanas asistieron más de doscientos delegados; en tanto que las sesiones del Congreso concurrieron más de mil personas de los Estados Unidos. Los trabajos y debates del cuerpo despertaron universal interés, pues indudablemente fué aquel la asamblea científica más grande que registra la historia del Hemisferio Occidental y probablemente la del mundo. Él fué, en consecuencia, digno continuador del Primer Congreso Cientifico Panamericano que en 1910 se reunió en la capital de Chile y de los que previamente y con una asistencia exclusivamente latino-americana se habían congregado en Río de Janeiro, Montevideo y Buenos Aires. Su éxito fué consecuencia lógica de las asambleas que anteriormente se habían reunido en la América latina y del cordial concurso que recibió de los gobiernos y de los hombres de ciencia de esa misma parte de América.

A cuantos no quisieren limitarse a consultar los volúmenes que contienen als memorias y los debates y desearen conocer algo más de las labores del Congreso y de los resultados por él alcanzados, se les recomienda la lectura del Acta Final y de la Exposición General concerniente a la misma que escribió el Dr. James Brown Scott, Informante General del Congreso, así como el Informe del Secretario General, prepa-

rado por el suscrito y por el Dr. Glen Levin Swiggett, Subsecretario General del mismo. En estos documentos podrán hallar no sólo el Acta Final y luminosas consideraciones acerca de la misma, sino también la nómina de los delegados y de los gobiernos, sociedades e institutos docentes que tuvieron representación en la Asamblea, juntamente con una relación puntualizada de las labores de la misma. Los que deseen obtener estos volúmenes pueden solicitarlos del Director General de la Unión Panamericana en Wáshington, D. C.

Como Secretario General del Congreso deseo hacer constar una vez más, antes de concluir, el agradecimiento que en mi informe general expresé por el cordial concurso que de todos recibí para asegurar el éxito del Congreso, desde el Presidente de los Estados Unidos y usted mismo como Secretario de Estado y desde los delegados de la América Latina y de los Estados Unidos hasta los diversos funcionarios del Congreso. El gran interés desplegado por la Comisión Permanente Ejecutiva, que presidió el Sr. William Phillips, a la sazón Tercer Subsecretario de Estado; por la Fundación Carnegie para la Paz Internacional, por el órgano de su Secretario, Dr. James Brown Scott; así como la colaboración del Dr. Glen Levin Swiggett, Subsecretario General, contribuyeron poderosamente a hacer memorable la asamblea. La Unión Panamericana, institución internacional sostenida por todas las repúblicas de América y cuyo Consejo Directivo está formado por los representantes diplomáticos latinoamericanos residentes en Wáshington y por el Secretario de Estado de los Estados Unidos, contribuyó con su poderosa influencia al éxito del Congreso y me autorizó para que desempeñara las funciones de Secretario General de aquél.

Con sentimientos de la más alta consideración me subscribo

De usted muy atento servidor,

JOHN BARRETT,
Secretario General.

Al Honorable SECRETARIO DE ESTADO,
Wáshington, D. C.

WASHINGTON, D. C., *Le 31 mai 1917.*

MONSIEUR: Conformément à la recommandation du Comité Exécutif du Second Congrès Scientifique Panaméricain qui a eu lieu à Washington du 27 décembre 1915 au 8 janvier 1916, et par la coopération du Congrès des États-Unis (loi du budget extraordinaire, 8 septembre 1916), les mémoires et discussions de cette grande réunion scientifique internationale ont été recueillis et édités pour être publiés sous l'habile direction du docteur Glen Levin Swiggett sous-secrétaire général. Ce volume contient le rapport de la section VIII, dont M. le Général W. C. Gorgas du Comité Exécutif était président.

Dans mon rapport officiel qui a été déjà soumis, je me suis étendu sur l'importance du Second Congrès Scientifique Panaméricain, sur le grand nombre de personnes qui y étaient présentes et sur l'excellence de ses mémoires et de ses discussions. C'est pourquoi, dans cette lettre qui, après avoir subi quelques changements sans importance, sert d'introduction à chaque volume, je n'en parlerai que d'une manière générale.

Toutes les républiques de l'Hémisphère Occidental au nombre de vingt-et-une étaient représentées au Congrès. De plus, des délégués à titre officieux envoyés par les associations scientifiques et les institutions éducatives les plus en vue de ces républiques ont soumis des mémoires et ont pris part aux délibérations. On peut donc considérer les mémoires et les discussions comme l'expression d'un grand effort scientifique panaméricain, possédant en conséquence une valeur inestimable.

Le Congrès était divisé en neuf sections principales que nous énumérons ci-dessous, en donnant le nom de leurs présidents.

I. ANTROPOLOGIE. W. H. Holmes.

II. ASTRONOMIE, MÉTÉOROLOGIE ET SISMOLOGIE. Robert S. Woodward.

III. Conservation des Ressources Naturelles, Agriculture, Irrigation et Forêts. George M. Rommel.

IV. Instruction Publique. P. P. Claxton.

V. Génie Civil. W. H. Bixby.

VI. Droit International, Droit Public et Jurisprudence. James Brown Scott.

VII. Mines, Métallurgie, Géologie pratique, et Chimie Appliquée. Hennen Jennings.

VIII. Santé Publique et Science Médicale. William C. Gorgas.

IX. Transport, Commerce, Finance et Impôt. L. S. Rowe.

A leur tour ces sections étaient subdivisées en quarante-cinq sous-sections.

On y comptait plus de deux cents délégués des républiques latino-américaines, et plus de mille délégués des Etats-Unis ont assisté aux réunions. Les discussions et les procès-verbaux du Congrès ont attiré l'attention du monde entier, et il a été sans le moindre doute la plus grande assemblée scientifique internationale de l'histoire de l'Hémisphère Occidental, et peut-être même du monde entier, qui se soit réunie jusqu'ici. Venant après le Premier Congrès Scientifique Panaméricain qui s'est réuni à Santiago, capitale du Chili, en 1908, et après ceux qui ont eu lieu précédemment, respectivement à Rio de Janeiro, à Montevideo et à Buenos-Ayres, ces derniers n'ayant que des représentants de l'Amérique Latine, il s'est montré leur digne successeur. Sa réussite a été un logique résultat de ces précédents concours dans l'Amérique Latine et de la sincere et cordiale coopération des gouvernements et des hommes de science de l'Amérique Latine.

Pour ceux qui n'ont porté leur attention que sur les volumes renfermant les mémoires et les discussions, et qui désireraient connaître d'une manière plus approfondie les actes et procès-verbaux du Congrès, ainsi que les résultats qui s'en sont suivis, je leur conseillerai de lire "L'acte Final, Commentaire explicatif," rédigé sous la direction du docteur James Brown Scott, rapporteur général du Congrès, et le rapport du Secrétaire Général rédigé par ce dernier et le docteur Glen Levin Swiggett. En les lisant on n'y trouvera pas seulement l'Acte Final et le commentaire explicatif, mais encore les listes des délégués, des gouvernements qui ont participé au Congrès, des sociétés, des institutions éducatives et autres, en même temps qu'un compte rendu soigné ainsi que l'histoire du Congrès. On peut se les procurer en faisant une demande par écrit au Directeur Général de l'Union Panaméricaine à Washington, D. C.

En terminant, je vais en qualité de Secrétaire Général du Congrès exprimer de nouveau en peu de mots mes remercîments, ce que j'ai déjà fait dans mon rapport officiel pour la part que chacun a eue dans la réussite du Congrès depuis le Président des États-Unis, vous comme Secrétaire d'État, les délégués de l'Amérique Latine et ceux des États-Unis jusqu'aux employés de bureau. Le haut intérêt manifesté par le Comité Exécutif permanent présidé par M. William Phillips, qui était alors troisième Sous-Secrétaire d'État, par la Fondation Carnegie pour la Paix Internationale, par l'entremise de son sécretaire le docteur James Brown Scott, et l'aide prêté dans l'exécution par le docteur Glen Levin Swiggett, comme sous-secrétaire général, ont puissamment contribué à faire de ce Congrès un événement mémorable. L'Union Panaméricaine, administration officielle internationale de toutes les républiques américaines, et dont le Comité d'Administration est composé des diplomates latino-américains à Washington et du Secrétaire d'État des États-Unis, a usé de sa favorable influence pour assurer le succès du Congrès et m'a autorisé, en qualité de Directeur Général de l'Union, à prendre en mains les responsabilités de Secrétaire Général du Congrès.

Veuillez agréer, M. le Secrétaire d'État, en même temps que mes respectueux hommages l'assurance de mon entier dévoûment,

John Barrett,
Secrétaire Général.

Monsieur le Secrétaire d'État,
Washington, D. C.

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FOREWORD.

The work of the hygienic section has been most valuable. It has already produced excellent results in causing the Rockefeller Foundation to undertake the work of exterminating yellow fever. All the South American countries affected by this disease have agreed to cooperate, and if it had not been for the European war the work would have now been well under way.

(Signed) W. C. GORGAS,
Chairman.

GENERAL SESSION OF SUBSECTION VIII.

NEW EBBITT HOTEL,
Monday morning, January 3, 1916.

Chairman, Surg. Gen. RUPERT BLUE.

The session was called to order at 9.30 o'clock by the chairman.

The CHAIRMAN. The session will please come to order. Dr. Goldberger is to present the first paper.

A RÉSUMÉ OF SOME OF THE RECENT STUDIES OF THE UNITED STATES PUBLIC HEALTH SERVICE RELATING TO THE CAUSATION AND TO A METHOD OF PREVENTING PELLAGRA.

By JOSEPH GOLDBERGER,
Surgeon, United States Public Health Service.

Introduction.—One of the outstanding features of the epidemiology of pellagra is the striking relation of the disease to poverty. In reflecting on this and in considering the elements that differentiate poverty from affluence, diet, in view of the conspicuous place it has always had in discussions of the disease, naturally arrested attention. Approaching the problem of the possible relation of diet to pellagra in this way, it seemed permissible to assume, on the one hand, that the diet of the poor—that is, of those who as a class are the principle sufferers from the disease—is for some reason pellagra-producing and, on the other, that the diet of the well-to-do, who, as a class, are practically exempt is, for some reason, pellagra-preventing. The thought was near, therefore, that it might be possible to prevent the disease by providing those subject to pellagra with a diet such as that enjoyed by well-to-do people. Early in 1914 it was proposed to put this idea to a practical test. Before this test was actually begun, studies of the prevalence of pellagra at institutions, such as prisons, asylums, and orphanages were made, the results of which, in the light of the recent advances in our knowledge of beriberi, very strongly suggested the idea that the disease was dependent upon a diet that was for some reason faulty, and that this fault was in some way either prevented or corrected by including in the diet suitable proportions of the fresh animal protein foods and legumes.[1]

[1] Prof. Voegtlin tells me that at about the same or even previous to this time, he had independently formed somewhat similar views which he presented in a paper read June 26, 1914, at the meeting of the American Medical Association, and published in the Journal of the American Medical Association, Sept. 26, 1914. The following quotations from this paper will give the student of the subject the essentials of Voegtlin's conception:

"From a survey of the clinical and pathologic aspects of pellagra, I have arrived at the conclusion that we are dealing with a chronic intoxication. While the agents at work in this intoxication are as yet unknown, I am inclined to believe that toxic substances exist in certain vegetable foods, not necessarily spoiled, which if consumed by man over a long period of time may produce an injurious effect on certain organs of the body. This hypothesis does not rule out the possibility that a dietary deficiency, * * * (vitamine) * * *, may play a rôle in the production and treatment of pellagra. Extensive feeding

These findings not only confirmed the original conception, but helped in defining this more clearly, and, moreover, made it possible to formulate more definite plans, which were temporarily broadened to include a test of diet in the treatment as well as in the prevention of the disease.

TREATMENT.

At the suggestion of the writer, Dr. W. F. Lorenz, who was at that time studying the psychiatric manifestations of pellagra at the Georgia State Sanitarium, treated a series of 27 cases in the insane at that asylum exclusively by diet. Considering the character of the cases with which he was dealing his results, as well as those of Dr. D. G. Willets, who for a time continued the work begun by Lorenz, were notably favorable.

When the various recent methods of treatment, each warmly advocated by its author, are critically reviewed in the light of the test made by Lorenz and by Willets, one can hardly fail to be impressed by the fact that the one thing they all appear to have in common is the so-called "nutritious diet," and it is difficult to escape the conclusion that it is to this single common factor that the marked success that is usually claimed for the "treatment" should properly be assigned.

It is of much interest to note that fully 50 years ago Roussel (Roussel, 1866, pp. 529–530), on the basis of long experience and from a critical review of the literature of his day, came to precisely the same conclusion. This is so much to the point that it is quoted herewith:

Without dietetic measures *all remedies* fail.[1] * * * When drugs and good food are simultaneously employed, it is to the latter that the curative action belongs; the former exercises simply an adjuvant action and is without approved efficacy except against secondary changes or accidental complications.

Hereafter the clinician who would attribute therapeutic value to any drug or other remedy in the treatment of pellagra should be prepared to show, what has not heretofore been done, that the curative effect claimed can not be attributed to the diet. It is true that the claim is not infrequently made that the beneficial effects of the remedy advocated were obtained without any change in diet. When the claim is critically considered, however, it amounts usually simply to this, that the observer gave no instructions as to a change in the patient's diet or assumes that such change as was made was too slight to merit consideration. It should not be overlooked that the symptoms of the disease (sore mouth, diarrhea) are very frequently such that the patient, entirely on his own initiative, may or does add or increase the proportion

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experiments which I have carried on during the last year with animals, such as mice, rats, and a few monkeys, on an exclusive vegetable diet, have shown that these lower animals develop certain gastro-intestinal symptoms, and sometimes die if put on an exclusive diet of corn, carrots, sweet potatoes, oats, etc. Symptoms arise often within three or four days, which point to the presence of an intoxication in these animals. Death resulted in some cases in a remarkably short time (three or four days). At necropsy constant lesions were found, such as hyperemia and hemorrhage in the gastro-intestinal canal. Sometimes the kidneys, lungs, and other organs show a congestion and slightly hemorrhagic condition. * * *

"It is probably more than a mere coincidence that the population of that part of the world in which pellagra is endemic lives on a mainly vegetable diet.

"The recent advances in the field of nutrition suggest new avenues of approach to the solution of this difficult problem. One will have to consider very seriously:

"1. A deficiency or absence of certain vitamins in the diet.

"2. The toxic effect of some substances, as aluminum, which occur in certain vegetable food. (The possible relation between aluminum and pellagra was also discussed in a recent monograph by Alessandrini and Scala, Contributo nuova alla etiologia e pathogenesi della Pellagra, Roma, 1914, which the author received at the time of proof reading. These investigators claim that colloidal silica contained in drinking water is one of the most important etiologic factors, inasmuch as they succeeded in producing lesions resembling pellagra in animals fed on water containing colloidal silica. Colloidal aluminum hydroxid or a mixture of colloidal silica and alumina produced the same results. In view of the fact, first discovered by us, that aluminum occurs in certain vegetable food in relatively large amounts, the work of the Italian authors furnishes additional evidence that aluminum occupies a prominent position in the etiology of pellagra.)

"3. A deficiency of the diet in certain amino-acids."

[1] Italics are Roussel's.

of the liquids (milk, eggs, broth) in his diet. And this may be done even before the physician is consulted.

Again, in order to substantiate the claims made for some particular remedy it is sometimes asserted that the patient's diet had all along included an abundance of the animal proteins and legumes. Careful inquiry in a number of such instances has almost invariably shown that what is meant in such cases is that either the family table was known or was assumed to be well supplied with these foods of which the patient was perhaps quite naturally assumed to have partaken abundantly. The important possibility that the patient by reason of a personal idiosyncracy or otherwise did not actually eat these foods is almost invariably overlooked. That these foods may in some degree enter into the pellagrogenous dietary calls, however, for no denial. The question always to be borne in mind is: Was it enough? The possibility, if not the probability, of a "twilight" zone within which a very slight change in any of the dietary components may cause an important shift of balance is not to be overlooked. In the present state of our knowledge, therefore, the question of a sufficient proportion can not in all instances be answered on the simple statement of the case. That as a matter of fact the proportion of the foods in question in these, which may be called borderland cases, was not enough is very strongly suggested by the favorable result of the simple expedient of having the patient continue the diet on which he is supposed to have subsisted, seeing to it, however, that there is actually consumed an abundance of the animal foods and legumes. This and the unsatisfactory progress of those patients who for one reason or another fail or refuse to cooperate in taking the diet is decidedly illuminating.

Such observations as the writer has been able to make strongly suggest that real recovery from an uncomplicated attack may not take place until after a minimum of about three or four months of full feeding of fresh animal proteins and legumes. But this should not be taken to mean that thereafter recurrences are impossible. A "recurrence," so-called, may conceivably take place after the lapse of any interval if there is a return for a sufficiently long period to a pellagrogenous—that is, "faulty"—diet. In pellagra, as in other conditions, the renewed operation of the essential causative factor may be expected to bring about a renewed manifestation of its effects.

PREVENTION.

In planning the test of the preventive value of diet it was decided to take advantage of the universally recognized fact that "normally" pellagra tends to recur in the individual from year to year.

In order to obtain as significant and decisive results as possible it was necessary to submit a large number of pellagrins to the test under known conditions. Fortunately, two orphanages were found in May, 1914, each having a high incidence of pellagra among its inmates. Later this preventive test was extended to include two groups of insane at the Georgia State Sanitarium.

In the study at the orphanages there was associated with the writer Asst. Surg. C. H. Waring, and in that at the Georgia State Sanitarium, Assistant Epidemiologist D. G. Willets.

Orphanage study.—The two orphanages at which the value of diet in the prevention of pellagra has been tested are located in Jackson, Miss. At both, cases of pellagra have been recognized for several years. During the spring and summer of 1914, up to September 15, a total of 209 cases of pellagra was observed in the children of these orphanages. Although a number of these at both institutions were known to be admission cases, others appeared to have developed first after considerable periods of residence, while a large proportion were in long-time residents. The factor or factors causing pellagra and favoring its recurrence seemed, therefore, to be operative at both institutions.

At both places hygienic and sanitary conditions left much to be desired. Both were overcrowded. Each drew and has continued to draw its drinking water from the public supply. One has a water-carriage sewerage system connected with that of the city; the other is provided only with unscreened privies. At the latter a great deal of soil pollution was noted.

Before beginning the test it was requested that no change be made in hygienic and sanitary conditions; this request, it is believed, has been fully complied with.

Since about the middle of September, 1914, the diet at both orphanages has in certain respects been supplemented by the Public Health Service. At both institutions a very decided increase was made in the proportion of the fresh animal and of the leguminous protein foods. The milk supply was greatly increased. The children between 6 and 12 years of age were provided with a cup of about 7 ounces of milk at least twice a day. Those under 6 had it three times a day. Until the spring of 1915 the milk used was all fresh sweet milk. In April of that year buttermilk was added to the diet; this was served at first only on alternate days to those over 12 years of age; later it was served to all at the midday meal. Eggs, which had not previously entered into the regular diet of these children, were served those under 12 years of age at the morning meal. It had been the custom to serve fresh meat but once a week; this was increased to three or four times a week.

Beans and peas, which had been conspicuous in the diet only during the summer and fall, were made an important part of nearly every midday meal at all seasons. No canned foods other than tomatoes were allowed. This was done in order to eliminate the possibly injurious action on the foods of the high temperatures to which they are necessarily subjected in the process.

The carbohydrate component of the institution diets was modified with the object of reducing the proportion of this element. In this connection it may be noted that though the corn component was much reduced it was not wholly excluded. Corn bread was allowed all children once a week and to those over 12 years of age grits once or twice a week in addition.

Of the 209 cases of pellagra observed at the two orphanages during the spring and summer of 1914, up to September, 1915, not less than 172 completed at least the anniversary date of their attacks under observation. In only 1 of these 172 pellagrins, following the change of diet, was there recognized during the year 1915 evidence justifying a diagnosis of a recurrence, although, on the basis of Rice's [1] experience at an orphanage in Columbia, S. C., there might reasonably have been expected some 58 to 76 per cent, or 99 to 130 of them, to recur. Furthermore there was observed no new case in any of the nonpellagrin residents, 168 of whom were continuously under observation for at least one year. Recent admissions aside, there has, during 1915, been no pellagra at one and but a single case at the other of these insitutions.

Asylum study.—Through the courtesy and with the very helpful cooperation of the officers and staff of the Georgia State Sanitarium, two wards of pellagrins, one in the colored and the other in the white female service, were made available for the test.

Large numbers of cases of pellagra are observed annually at this institution, the largest in the South. A large proportion of these are admission cases, but cases of intramural origin are of frequent occurrence. This asylum must, therefore, be regarded as an endemic focus of the disease.

The wards were organized for this test late in the fall of 1914. In selecting the patients only one condition was observed, namely, that the patient should be of such a type as would give reasonable degree of probability of remaining under observation for at least a year. In consequence a considerable proportion were of a much deteriorated, untidy class.

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[1] Goldberger, Waring, and Willets 1915 b, P3126

The diet furnished the inmates of these two wards was, as at the orphanages, supplemented by the Public Health Service and modified so as to increase decidedly the proportion of the animal and leguminous protein elements. A cup of about 7 ounces of sweet milk is furnished each patient for breakfast and one of buttermilk at both dinner and supper. Fully half a pound of fresh beef and 2 to 2½ ounces of dried field peas or dried beans enter the daily ration. In order to favor the consumption of milk, oatmeal has almost entirely replaced grits as the breakfast cereal. With a view of reducing the carbohydrate component, sirup has been entirely excluded. Corn products, although greatly reduced, have not been entirely eliminated. The menu that follows will serve to give a more detailed idea of the character of the diet furnished:

WEEKLY MENU.

Monday.—Breakfast: Grits, sweet milk, sugar, broiled steak, hot rolls, biscuits, coffee. Dinner: Roast beef, gravy, peas, potatoes, rice, biscuits, buttermilk. Supper: Stewed apples, light bread, coffee, buttermilk, sugar.

Tuesday.—Breakfast: Oatmeal, sweet milk, sugar, hamburg steak, biscuits, hot rolls, coffee. Dinner: Beef stew, potatoes, rice, bread, buttermilk. Supper: Baked beans, light bread, coffee, sugar, buttermilk.

Wednesday.—Breakfast: Oatmeal, sweet milk, sugar, beef hash, hot rolls, biscuits, coffee. Dinner: Pea soup, corn bread, gravy, potatoes, rice, bread, buttermilk. Supper: Stewed prunes, light bread, coffee, sugar, buttermilk.

Thursday.—Breakfast: Oatmeal, sweet milk, sugar, fried steak, hot rolls, biscuits, coffee. Dinner: Beef stew, peas, potatoes, rice, bread, buttermilk. Supper: Baked beans, bread, coffee, sugar, buttermilk.

Friday.—Breakfast: Oatmeal, sweet milk, sugar, broiled beefsteak, hot rolls, biscuits, coffee. Dinner: Pea soup (purée), roast beef, potatoes, rice, bread, buttermilk. Supper: Light bread, coffee, sugar, buttermilk, apples, baked beans.

Saturday.—Breakfast: Oatmeal, sweet milk, sugar, hamburg steak, hot rolls, biscuits, coffee. Dinner: Beef stew, potatoes, rice, bread, buttermilk. Supper: Bread, baked beans, buttermilk, coffee, sugar.

Sunday.—Breakfast: Oatmeal, sweet milk, sugar, mackerel, bread, coffee. Dinner: Loaf beef and gravy, peas, potatoes, rice, bread, buttermilk, pudding. Supper: Beef hash, bread, sugar, coffee, buttermilk.

NOTE.—Green vegetables in season at irregular intervals. Milk and eggs, as a special diet, are furnished those patients who may require them.

Aside from the modification in the diet and the increased watchfulness over the individual feeding, enjoined on the nurses and attendants, no change in the habitual routine of the corresponding services was made.

Of the pellagrins admitted to these wards at the time of their organization, or shortly thereafter—that is, up to December 31, 1914—72 (36 colored and 36 white) remained continuously under observation up to October 1, 1915, or, at least, until after the anniversary date of their attack of 1914. Of the colored patients, 8 have histories of at least 2 annual attacks; of the white patients 10 have histories of at least 2 attacks. Nevertheless not a single one of this group of 72 patients has presented recognizable evidence of a recurrence of pellagra, although of a group of 32 control pellagrins (17 colored and 15 white) not receiving the modified diet, 15 (9 colored, 6 white), or 47 per cent, have had recurrences during the corresponding period.

Significance.—Considering the foregoing results as a whole, bearing in mind that three different institutions are involved, each institution an endemic focus of the disease, and bearing in mind also that the number of individuals is fairly large it would seem that the conclusion is justified that the pellagra recurrence may be prevented and, in view of the conditions of the experiment, that it may be prevented without the intervention of any other factor than diet. In this connection the ques-

tion arises whether it is permissible to extend this conclusion to the primary attack, apart from its recurrence. The character of the answer to this question will depend on the view held as to the nature of the pellagra recurrence.

Among the epidemiological features of pellagra none is more striking than the tendency for the disease not only to develop in spring or early summer, but to recur year after year at about the same season. Various explanations of this singular phenomenon have been advanced. According to Sambon (1910, p. 49), "this peculiar periodicity of symptoms can be explained only by the agency of a parasitic organism presenting definite alternating periods of latency and activity." A somewhat similar conception appears to be held by the Thompson-MacFadden Commission (Siler, Garrison, and MacNeal, 1914c), who distinguish between conditions favorable for the development of the disease, in the first place, and those that permit its subsequent recurrence. Why these and many other observers should consider this periodicity of symptoms as explicable only by the agency of a parasitic organism or of a virus or a toxin presenting definite alternating periods of latency and activity is rather hard to understand when it is recalled that in endemic scurvy (Lind, 1772, pp. 33, 84, 130, 306), and particularly in endemic beriberi (Scheube, 1903), diseases of well-known dietary origin, a strikingly similar periodicity is present. It would seem, therefore, entirely permissible to invoke as an explanation of the periodic recurrence in pellagra what undoubtedly is the explanation of the same phenomenon in these other diseases, namely, a modification or change in diet brought about by or incidental to the recurring seasons. Viewed in this light, the recurrence in pellagra may be considered as in beriberi, etiologically at least, as essentially identical with the initial attack, and, therefore, it would seem permissible to conclude that the means found effective in the prevention of recurrences will be found effective in the prevention of the initial attack.

NATURE OF DISEASE.

In the course of the preliminary studies relating to the prevalence of pellagra at such institutions as prisons, asylums, and orphanages, to which reference was made early in this paper, the association was found of a very high incidence of pellagra, restricted to certain groups, with a diet which differed from the diet of the exempt groups so far as could be determined only in that it included minimal quantities of the animal foods. It was inferred at that time that this association had etiological significance. Advantage has been taken of an opportunity to put this inference to the test of experiment.

The experiment was carried out in association with Asst. Surg. G. A. Wheeler at the farm of the Mississippi State Penitentiary, about 8 miles east of Jackson, Miss.

At about the center of this farm of some 3,200 acres, well isolated from the surrounding community, is the convict camp. There is no history of the previous occurrence or presence of pellagra on this farm. During the period of the experiment there were quartered at the camp an average of between 70 and 80 white male convicts, of whom some 30 were present throughout this time. Through the kind offices of Dr. E. H. Galloway, secretary of the Mississippi State Board of Health, the interest of Gov. Earl Brewer was enlisted, who, on the offer of a pardon, obtained 12 volunteers for the test.

Experiment.—White adult males were selected because, judged by the incidence of the disease in the population at large, this age, sex, and race group would seem to be the least susceptible to the disease.

The "pellagra squad," as it came to be called, was organized between February 1 and February 4, 1915, with 12 volunteers. On July 1, 1915, one of the squad was released because of the development of a physical infirmity. This left 11 men in the squad, 24 to 50 years of age, who remained in the test to its termination, October 31, 1915. These men were quartered in a small, practically new, screened cottage,

about 500 feet from the "cage" in which the other convicts were domiciled. Part of this cottage had previously been used, and continued to be used, throughout the period of the experiment as quarters for one of the officers of the camp. From the time of its organization the squad was segregated and under special guard.

From February 4 to April 19, 1915, a period of 2½ months, these men were kept under observation without any change in the regular prison fare. Having detected no evidence of pellagra during this preliminary observation period, the diet of the squad was changed at noon April 19, 1915. The ingredients of this diet were wheat flour (patent), corn meal, (corn) grits, cornstarch, white polished rice, standard granulated sugar, cane sirup, sweet potatoes, pork fat (fried out of salt pork), cabbage, collards, turnip greens, and coffee. In the preparation of the biscuits and of the corn bread Royal baking powder was used.

The quantities of the different articles of cooked food actually consumed is illustrated by the following for the week ended August 8, 1915:

Biscuits, 41.81 pounds; rice, 24.25 pounds; corn bread, 24.56 pounds; grits, 27.06 pounds; fried mush, 33.87 pounds; brown gravy, 37.81 pounds; sweet potatoes, 23.62 pounds; cabbage, 4.25 pounds; collards, 23.75 pounds; cane sirup, 5.94 pounds; sugar, 8.75 pounds, making a total of 255.67 pounds of food consumed during the week, or 3.32 pounds per man per day, having a value of 2,952 calories.

In this connection it may be pertinent to note that the corn meal and grits were of the best quality obtainable at the local market and the same as that used at one of the orphanages at which the test, already discussed, of the value of diet in prevention was made and at which no pellagra occurred this year. Except for one meal in which 4 ounces of meat were included the animal proteins and legumes were almost entirely excluded.

The character of the labor performed by these men during the week for which the statement of the quantity of food consumed has been given was as follows: Whitewashing fences and buildings, 2½ days; sawing lumber (ram sawmill), 2 days; rest, 2½ days.

The volunteers kept about the same hours and did about the same kind of work as the other convicts. The amount of labor performed by the volunteers was, however, distinctly less than that by the other convicts.

The general sanitary environment was the same for volunteers and controls. With respect to personal cleanliness, cleanliness of quarters, freedom from insects, particularly bedbugs, flies, amd mosquitoes, the volunteers were decidedly better off.

Results.—Of the 11 volunteers not less than 6 developed symptoms, including a "typical" dermatitis, justifying a diagnosis of pellagra. Loss of weight and strength and mild nervous symptoms appeared early. The gastrointestinal symptoms were slight. Definite cutaneous manifestations were not noted until September 12, or about five months after the beginning of the restricted diet. In all 6 cases the skin lesions were first noted on the scrotum. Later the eruption also appeared on the hands in 2 of the cases, and on the back of the neck in 1. The scrotal lesion conformed to the type described and figured by Merk (1909, p. 24, fig. 6), and also by Stannus (1913).

Although the entire population of the camp was kept under observation, no one, not of the volunteer squad, presented evidence justifying even a suspicion of pellagra.

The diagnosis of pellagra was concurred in by Dr. E. H. Galloway, secretary Mississippi State Board of Health, and Dr. Nolan Stewart, formerly superintendent Mississippi Asylum for Insane, at Jackson. In excluding the other known dermatoses the expert knowledge and skill of Prof. Marcus Haase of the Medical College of the University of Tennessee, Memphis, Tenn., and of Prof. Martin F. Engman of the Washington University Medical School, St. Louis, Mo., was utilized in consultation.

Conclusions.—The conclusion drawn from this experiment is that pellagra has been brought about in at least 6 of the 11 volunteers as the result of the one-sided diet on

which they subsisted. Taken in conjunction with the striking results of the test of the preventive value of diet, the further conclusion seems justified that pellagra is essentially of dietary origin.

In order to avoid misunderstanding it may be well to point out that it does not necessarily follow that all one-sided, unbalanced or, as the writer prefers for the present to speak of them, faulty diets are capable of bringing about pellagra any more than they are of bringing about scurvy or beriberi.

A definite conclusion as to the intimate mechanism involved in bringing about or in preventing the disease by diet can, of course, not be drawn from the available data. It would be premature to conclude that pellagra is necessarily due to a lack or deficiency of fresh animal or leguminous protein foods. Clearly, however, the dietary "fault" upon which the production of pellagra essentially depends is capable of being corrected or prevented by including in the diet a suitable proportion of these foods. It would be equally premature, moreover, to assume that the pellagra-causing dietary "fault" is capable of correction in this way only. The possibility that there may be other foods capable of serving the same purpose is by no means to be overlooked. It may be, too, if Funk's suggestion that pellagra is a vitamine deficiency, brought about by the consumption of overmilled corn, is proven to be correct, that the use of undermilled corn will of itself correct the "fault" in a diet in which this cereal is the staple. There is to be considered also Voegtlin's explanation of the beneficial effect of a liberal diet on the course of the disease. Voegtlin suggests that by substituting for part of the vegetable food animal foodstuffs, the absolute amount of vegetable products consumed will be reduced considerably and thus probably also reduce the possibility of an injurious action of the vegetable food on the body, particularly the irritant action on the gastrointestinal canal. On the whole, however, the trend of available evidence strongly suggests that pellagra will prove to be a "deficiency" disease very closely related to beriberi.

For the practical purposes of preventive medicine, the point of chief of fundamental importance would seem to be the recognition of the fact that the pellagra-producing dietary fault, whatever its intimate nature, or however brought about, is capable of correction or prevention, as the results of the studies above summarized clearly indicate, by including in the diet suitable proportions of the fresh animal and leguminous protein foods.

SUMMARY.

1. Diet is the common factor in the various methods of treatment recently advocated. The marked success claimed for each of these methods must logically be attributed to the factor (diet) which they have in common.

2. The value of diet in the prevention of pellagra has been tested at two orphanages and at an asylum for insane, endemic foci of the disease. Marked increases in the fresh animal and leguminous protein elements of the institution diets were made.

Of 209 cases of pellagra observed at the two orphanages during the spring and summer of 1914, not less than 172 completed at least the anniversary date of their attack under observation. In only one of these 172 pellagrins, following the change in diet, was there recognized evidence of a recurrence, although on the basis of experience elsewhere some 99 to 130 might reasonably have been expected. Nor was any new case observed among the nonpellagrin residents, 168 of whom completed not less than one year under observation.

Of the group of pellagrins on the modified diet at the insane asylum, 72 remained continuously under observation up to October 1, 1915, or at least until after the anniversary date of their attack of 1914. Not one of this group has presented recognizable evidence of a recurrence, although of a group of 32 controls 15 have had recurrences. Pellagra may, therefore, be prevented by an appropriate diet without any alteration in the environment, hygienic or sanitary, including the water supply.

3. At an isolated convict camp, previously free from pellagra, with an average population of 70 to 80 white males, 11 volunteers were segregated and, after a preliminary observation period of 2½ months, placed on an abundant but one-sided, chiefly carbohydrate (wheat, corn, rice) diet, from which fresh animal proteins and legumes were excluded. At least 6 of these volunteers developed pellagra. This result would appear to have been brought about by the diet on which they subsisted.

4. A definite conclusion as to the intimate mechanism involved in bringing about or in preventing the disease by diet can not be drawn from the available data.

5. For the practical purposes of preventive medicine it would seem to be of fundamental importance to recognize that the pellagra-producing dietary fault, whatever its intimate nature or however brought about, is capable of correction or prevention by including in the diet suitable proportions of the fresh animal and leguminous protein foods.

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The CHAIRMAN. Dr. Goldberger's paper is open for discussion.

Dr. AGRAMONTE. The question of pellagra in South and Central America is still, I believe, to be investigated. So far as I know, pellagra has not been observed in Cuba. That may be accounted for to a certain extent—discounting the possibility of unrecognized cases, which, of course, must be considered—by the fact that the diet in our country is quite abundant in leguminous food, particularly beans, which form a usual part of the menu almost everywhere, and as for the orphanages and asylums either corn or beans form a daily part of the diet. The fact that is pointed out by Dr. Goldberger and well known to those who have studied this question, viz., that the disease untreated tends to recur, would serve to do away with the idea of the disease passing unrecognized amongst us. If we did not think of it the first time, I think our attention would have been called to it the next time or at a subsequent time, so I feel safe in stating that we have no cases of pellagra, at least in our public institutions.

About three years ago I had occasion to see a few cases of pellagra in London, shown to me by Dr. Sambon at the time when he claimed that the simulium was the cause of the disease, and he explained the reason of these recurrences by calling attention to the fact that the recurrence took place during the warmer part of the year, when the parasitic nature of the disease seemed more in condition to develop. Of course that has all been explained by Dr. Goldberger, and the argument alone would not be sufficient to do away with all other arguments.

The CHAIRMAN. Is there anybody else? I see that Capt. Siler, of the Robert M. Thompson Pellagra Commission, is here.

Capt. J. F. SILER, M. C., United States Army. I think we should all congratulate Dr. Goldberger on the very thorough way in which he has demonstrated that we can cure and prevent pellagra by dietary changes. I think those of us who have treated pellagra have been very much struck by the fact that a very large percentage of the victims have been living on a restricted diet, and also that recovery would occur in a very large majority of cases by putting them on the proper diet. I suppose that in the three years I was working with pellagra I have probably answered two to three hundred letters from patients who had it, and my advice was always to treat the disease as if it were tuberculosis; that is to say, to build up the

nutrition by the use of eggs and milk particularly; and though such a diet did not give results in all individual cases, in a large majority of cases the results were good.

One point to which I wish to refer is the disappearance of pellagra in institutions and in communities. We made epidemiological studies in Spartanburg County, S. C., as well as other places in this country and abroad, and we found it to be not unusual to have a large amount of pellagra in a community one year and very little or none the following year. We had a number of instances of that kind. There is a mill village near Spartanburg, S. C., in which in 1910 or 1911 you could go out any day and find 50 or 60 cases of active pellagra. In 1914 there were only two or three cases in that village. So far as we could determine, no particular dietary changes had been made in that time. There was a very distinct tendency to better conditions in the way of improved hygiene and sanitation, but we could not lay our finger on any particular change or changes to which we could attribute the marked decrease in incidence.

In 1913 I made a trip with Dr. Sambon, of London, to the British West Indies, including Jamaica and Barbados. In Jamaica, curiously enough, the disease appeared to be confined to two or three institutions. We examined several thousand people in villages and institutions in all parts of Jamaica, and found pellagra prevailing in but two institutions—the asylum and a home for children. The diet in the children's home was very poor, but even so it was better and more varied than the inmates were getting before they went into the home. In 1913, when we made this trip, between 10 and 15 per cent of the children in this home were affected. I have heard recently from authoritative sources that during the past two years they have made no changes in the dietary, only giving tonics, and the disease has disappeared. We have noted repeatedly in our epidemiological studies that the incidence rate has a tendency to go up one year and down the next.

I also noticed in investigating conditions in the West Indies that individuals who were living on an improper and poorly balanced diet, presented all the evidences of undernourishment, and one of the striking evidences presented by them was interference with the nutrition of the skin. Dr. Sambon wished to class these as pellagra, though the skin symptoms were somewhat atypical. I did not agree with him for the reason that I could in no instances get a history of, nor did I personally observe any individuals with the gastro-intestinal symptoms so common in pellagra. In Barbados, when going through the poorer sections of Bridgetown, by house-to-house canvass, and in Jamaica, we saw many cases which seemed to me to fit the ones that Dr. Goldberger has described to-day as occurring in the convicts. I particularly wish to ask him just what the gastro-intestinal symp-

toms were that he refers to. It seems to me that in a crucial test of this kind, where people have been on a so-called pellagra-producing diet for the length of time these convicts were, he ought to have gotten two or three cases with at least moderate but typical intestinal symptoms so frequently observed with pellagra. The cases that I saw in Barbados and Jamaica that presented somewhat atypical skin lesions resembling pellagra, gave no definite gastro-intestinal symptoms, and in not a single case did I see the picture so frequently found in pellagra of a severe stomatitis.

There are many observations that lead me to feel that it is quite possible that some etiological factor in addition to dietary faults enters into the production of pellagra. Dr. Goldberger has demonstrated very clearly that the way to cure pellagra and to prevent pellagra in practically all cases is to give the proper food. In considering all the factors entering into the causation of pellagra, there are some things that seem to me to be difficult of explanation on a dietary hypothesis alone. One of these is the recent appearance of pellagra in this country. There is no question that pellagra has been in this country for the last 15, 20, 30, or even 40 years; but I think there is also no question that about 1906 or 1907 it began to increase very rapidly in the United States. We are told that the explanation of this is that we began to recognize it then. I do not believe that. I have no doubt that many cases were missed in the early days, but I believe that there is no doubt that the disease has increased tremendously in very recent years.

One of the arguments advanced against calling pellagra an infection is that doctors and nurses are presumed never to have been affected by it, though thrown with it constantly. Personally, I know of about five cases among nurses, certainly of that number among nurses employed in institutions. I know also of about twelve or fifteen doctors in the South who have, or have had pellagra. Pellagra and tuberculosis are, in my opinion, comparable in many respects; and we might with just as much logic argue that tuberculosis is not an infection because doctors and nurses working with tuberculosis so seldom acquire it. In the very excellent paper presented by Dr. Ravenel, before this congress last week, he laid particular stress on the fact that statistics show very conclusively that tuberculosis is but seldom acquired by nurses and doctors working in sanitariums for tuberculosis or by nose and throat specialists who are constantly being thrown in contact with cases of laryngeal tuberculosis. I have had occasion to observe the incidence of tuberculosis in doctors and nurses working with such cases, and these observations are confirmatory of those cited by Dr. Ravenel.

One thing that has struck me is this: I have seen a number of cases of the very severest type of pellagra that, during the acute attack,

adhered to a proper diet—that is to say, an increase in protein, more particularly milk and eggs—and recovered from the acute attack with no recurrence in after years, notwithstanding the fact that they have gone back on the same diet on which they lived before they had pellagra. I have gone into the diet of a number of people who have given such a history, and it is somewhat hard for me to understand how a person who has had a disease of a dietary nature can avoid a recurrence on a return to the original diet causing the disease. In beriberi, we know that if one returns to the beriberi-producing diet, he is very likely to acquire the disease again. I have seen a number of pellagrins after severe attacks return to what is theoretically a pellagra-producing diet for two or three years or more without the slightest evidence of recurrence of the disease, and it is very difficult for me to explain this subsequent immunity on the dietary hypothesis.

I have also seen this happen: Two cases would go into a hospital side by side—one a very mild case of pellagra in which we wanted to build up the resistance by the use of eggs and milk; the other a case of such great severity that food could not be swallowed for several days. We would put them on the same diet and at the end of a month or six weeks the mild case would be dead and the other practically well. You see a thing like that not infrequently.

I have also seen some cases where, though it could not be claimed that the diet was perfect from the viewpoint of the dietary enthusiast, it seemed to me to be very well balanced indeed.

In our epidemiological studies we have noticed the factor of distribution according to race. In the particular section in which we were working we found that the relation existing between the colored race and white race was about one to four, certainly one to three—that is, three white persons had pellagra to every colored person. The diet, in my opinion (and I have lived in the South; I may say spent my whole life there until manhood), of the colored tenant farmers in the section in which we were working more nearly approximated the diet given the convicts in this test than that of the white people of the same section, notwithstanding that the proportion of pellagra in that region was about one to three. If you will investigate conditions in Charleston, S. C., you will find the racial distribution reversed; there are three cases of pellagra among the colored population to every case among the whites. We investigated this point in Alabama, and found that in Montgomery the disease is evenly distributed between the negroes and the whites. In formulating any hypothesis as to the etiology of pellagra these factors require consideration.

In discussing diet as a factor in the causation of pellagra, and particularly the matter of proteins, I recall that several years ago in the State of Illinois a commission was appointed by the governor to investigate pellagra in the institutions of the State. I think a good

many people have overlooked the fact that this commission reported that among the institutions of the State the one in which the protein content of the diet was lowest never had had a case of pellagra.

There are some other points to which I desire to refer. In my work on pellagra I have had in mind beriberi and scurvy—our two well-known deficiency diseases—and have constantly attempted to connect the epidemiology of beriberi and scurvy with the epidemiology of pellagra. For instance, it is said and we know that nursing children are very subject to beriberi. In pellagra I have never seen a case in a child nursing its mother, although the mother might have a very severe case of pellagra. This is another respect in which pellagra differs very markedly from beriberi.

The age and sex distribution are also of great interest to me. Dr. Goldberger has spoken of the remarkable fact that women are very much more subject to pellagra than men. In 1913 we had collected a series of 740 cases, of which in a group of 414 between the ages of 20 and 44 there were 357 women as against 57 men. This is most remarkable, in my opinion, in comparing the disease with beriberi. So far as I can determine from mortality statistics, beriberi is more evenly distributed. It might be argued that the men in the home are getting the best diet, but I have investigated the homes of the people most subject to pellagra and they do not have meat every day, so the men could not get it. If they have not the proper food on their tables, how can they get it, and how do the tremendous number of men escape the disease?

This is a very haphazard discussion, but I should like to ask Dr. Goldberger if he has ever gotten any negative results that seemed to him to indicate the possibility of its not being a food deficiency alone. For example, has he ever made any observations on people who have had pellagra who have gone through two or three attacks and, notwithstanding the fact that they have been kept on a presumable pellagra-producing diet have not had the disease? In children we have found that it does not recur in 50 per cent, possibly more, of the cases. They have an attack one year, and that is the end of it.

I was very glad to hear Dr. Goldberger's discussion about this disease, and I should like very much to hear the experiences of doctors from the Central and South American countries. I might say that as far as Jamaica and Barbadoes are concerned, and also Bermuda, I have some knowledge. In Jamaica the disease was confined practically to a few institutions, hardly a dozen cases, I believe, outside of institutions. In Barbadoes it was scattered generally over the island. There had been 200 deaths from pellagra in the two years prior to 1913. The only particular difference in the diet of the natives of Jamaica and Barbadoes was that in Jamaica

the peasants had bananas and in Barbados they did not. This dietary difference is of interest in connection with Maj. Ashford's observations on sprue. He noted that sprue occurred in the cities and towns of Porto Rico, where the carbohydrate element of the diet was made up of bread, and it did not originate in the country districts where the peasant secured his carbohydrates by eating bananas. In Barbados sprue is very common and wheat bread is the staple carbohydrate food. In Jamaica sprue is very rare, and the peasants subsist very largely on bananas.

With regard to the use of legumes, we found that they were consumed with great frequency by the people of the Southern States. In Jamaica and in Barbados, as Dr. Agramonte has said, they use leguminous foods very largely. In Barbados, where there is much pellagra, the people have 15 to 20 varieties of beans and peas, which are eaten throughout the year. We know also, if we can believe what we hear about the diet of the people, that in Egypt the fellaheen use legumes as one of the staple articles of diet. We also know that the fellaheen are extremely susceptible to pellagra.

Capt. Siler's remarks were interpreted in Spanish by Dr. Agramonte.

Dr. Goldberger's paper was discussed further in Spanish by Dr. Gonzalez-Rincones, of Venezuela; Dr. Teodoro Muhm, of Chile; Dr. Calixto Torres Umaña, of Colombia; and Dr. Luis Migone, of Paraguay. The remarks of these gentlemen were interpreted as follows by Dr. Agramonte:

Dr. Rincones has practically determined the absence of pellagra in his country. He refers to several cases which he has had occasion to see, but which turned out to be cases of uncinaria; and recognizing the importance of Dr. Goldberger's findings with regard to the treatment of the disease by the change of diet, he is inclined to attribute the absence of this disease to the fact that legumes are used largely. He says the observations have an indirect bearing on cases of infectious disease in relation to improving the general condition of the individual and thereby allowing him to overcome the disease, and that he has decided to employ the treatment as soon as he has an opportunity to do so.

Dr. Muhm, of Chile, recalls no case of pellagra in his country.

Dr. Torres Umaña, of Colombia, recalls that he has seen no classical case of pellagra, although he has found cases similar to pellagra, produced by the use of a drink which is called "chicha," obtained by the fermentation of corn to such a degree that it contains actual putrefactive element. The individuals who use this drink present disturbances of nerves, skin, and gastro-intestinal tract, very much like pellagra. He considers they are exactly like the classic pellagra.

Dr. Migone, of Paraguay, remarks that no cases of pellagra are, to his knowledge, found in his country. Once a year the doctors from the interior meet in the form of a congress and discuss unusual cases that have come to their notice, and that in so far as he knows pellagra has never been reported. He states that maize, corn, and many vegetables are consumed in most tropical and semitropical countries in great quantity by every one.

Dr. KEBLER. I was rather interested in what Dr. Goldberger has said relative to the effect, if any, of drugs in the treatment of pel lagra. According to the view taken by Dr. Goldberger, drugs have no influence. Dr. Siler, however, seemed to give the impression, whether he means it or not, that tonics might be of value in the treatment of this disease, when he stated that in a certain institution there was virtually no change in diet, but that tonics had been added and that improvement took place. We have made an investigation of quite a number of these so-called cures for pellagra on the market, and as in the case of nephritis, tuberculosis, and other diseases, it is quite a problem in these cases to decide just what to do.

Dr. SILER. May I explain myself, Mr. Chairman? I did not say that drugs were of any value. I did say that they were using tonics in this institution in Jamaica. The drug they were using there was salvarsan. I would like to have it distinctly understood that I agree with Dr. Goldberger that drugs really do no good in pellagra. Diet is the most important thing and I place no reliance at all on drugs. There are two drugs that are indicated in these cases. There is no doubt that most cases of pellagra have a distinct decrease in hydrochloric acid and a decrease in peptic activity, and I think as a kind of placebo indicated in those cases where you have such factors in the stomach it is wise to give those drugs to increase the digestive action. That is about all that is really necessary—pepsin and hydrochloric acid.

The CHAIRMAN. Dr. Goldberger will close the discussion.

Dr. GOLDBERGER. I have been very much interested in what the delegates from the other countries have had to say about pellagra in their respective Republics. I might say, as the result of some correspondence with colleagues in Mexico City, that I have found conditions there as regards prevalence about the same as in these other countries. There is apparently no pellagra in Mexico. I learned of one case in Mexico City, that occurred a few years ago in a native and resident of the plateau region of Mexico. There have been no cases (up to 1914) in the "Manicomio," the National Insane Asylum at Mexico City, although corn, and spoiled corn, have formed at times a very large and important part of the diet. My correspondent who was in a position to speak authoritatively, stated that if pellagra was the result of spoiled corn there should have been no nonpellagrins in that institution.

While I believe these reports to be substantially correct, I must nevertheless confess to a certain degree of skepticism as to the absolute absence of the disease, an idea that one might get from these reports. I say that because I have very keenly in mind the pellagra history in our own country. Unquestionably it has occurred and has prevailed in this country for many years. It has, however, only been definitely recognized in the last eight years, and even now after all the publicity that this subject has had in the medical and the lay press cases are constantly occurring and are being seen and passed over by physicians without recognition. I know of instances of that sort in the hands of very competent and able men in other respects.

That brings me to the point raised by Dr. Siler in connection with the experimental cases at Jackson, at the State farm. Now, in the diagnosis of a disease like pellagra, concerning which we have no laboratory methods of diagnosis, there is left a great deal to the personal point of view, to the conception or mental picture that the observer has, to which the case must conform to be classed with this disease. We have the same sort of thing in other diseases, notably in connection with yellow fever. You will recall that in cities where the first case was reported or was about to be reported, or where there was danger of its being reported, unless the patient had all the classical symptoms of black vomit, profound jaundice, suppression of urine, etc., it was not yellow fever. Now the same thing undoubtedly applies to a greater or less degree to pellagra. Unless the individual has a marked eruption, unless he has a severe stomatitis with nausea, vomiting and continuous diarrhea with marked mental manifestations in the opinion of some men it is not a case of pellagra.

Now I think we ought to know a little more in this day and generation about any disease. As with other diseases, pellagra varies and does not in most instances manifest the so-called classical picture in cross section.

The following subjective manifestations were presented by our cases at the farm: There was observed marked loss of weight and strength, slight burning of the mouth, some redness of the tongue, eructations and dyspeptic symptoms and irregular, brief periods of looseness of the bowels. Not any of the cases, as I stated in my paper, showed the classical, complete gastro-intestinal symptoms—that is, severe salivation or sore mouth, with severe diarrhea. They were cases that had not gone that far. We were obliged to terminate the test by a certain fixed date. Fortunately, both we and a number of experienced consultants were able to satisfy ourselves that it was pellagra that our subjects had. The skin manifestations had the classical anatomical characters. They conformed, as I stated, to some of the pictures given by Merk in his "Handbuch";

they conformed very beautifully to some of the observations made by Stannus on pellagra in Nyassaland.

The illustrations of the eruption on the male genitalia in Merk and in Stannus give an excellent idea of what we observed in our experimental cases and are sufficient to indicate that what we saw in our experimental cases had been seen by others in other places under natural conditions. Nor should it be forgotten that we had a large number of controls, both convicts and free men and women, none of whom showed the least suspicion of the disease.

A number of points were raised by Dr. Siler that are very frequently raised in the discussion of pellagra, and it may be perhaps well to take up these things as fully as my time will allow. One of these points that is very frequently raised is the question of the explanation of the marked increase in the prevalence of the disease in this country in the last seven or eight years. As I mentioned, pellagra undoubtedly has prevailed in this country for a generation or more. Dr. Babcock, of Columbia, S. C., reports that he has been able to find records of the disease as far back as 1828, quite far enough back to establish that it has existed among us for a long time. The question to be answered then is, why is it so much more prevalent than it used to be? This probably may be explained in two or three ways, or rather two or three factors enter into the explanation. One of these is that when we know a disease we are better able to diagnose it. Those of you who are familiar with the classical manifestations of the disease, know it has many relations, side chains, if you will; the dermal manifestation is allied closely to other non-pellagrous dermal manifestations, and one without a complete picture of pellagra in his mind will be inclined to consider it simply a skin disease, to call it dermatitis, eczema, or erythema solare, and let it go at that, without paying due regard to the other symptoms, just as some of the earliest students of the disease did.

Again, the intestinal symptoms are sometimes very prominent and dominate the picture, and to the inexperienced observer, who is not familiar with the complete syndrome, that feature will concentrate attention, and the case will be called dysentery or "consumption of the bowels," a very favorite diagnosis in this country. It is the same way with the mouth symptoms. It is reported in the early American literature on the subject that a very distinguished clinician of this country who saw a case in consultation after a very careful investigation decided that it was a case of "glossitis." It is said to have been a typical case of pellagra. I mention these things to show how important a clear conception of a disease is in making a diagnosis. Improved diagnosis makes for an increase in known or reported cases; an increase that may be more apparent than real. Incidentally this also brings about a reduced fatality rate and then we hear that the disease has become milder.

I might cite evidence also to show the importance of knowing of the existence of a disease to help one recognize it, and thereby further increase the apparent frequency of its prevalence. One factor, then, in explanation of the increase in prevalence is the better diagnosis of cases, an increased ability to recognize the disease as the result of increased experience and because of a knowledge of its existence. This same factor applies also to the laity. The laity have learned to recognize pellagra, and frequently the patient comes to his physician for a confirmation of the diagnosis which the patient or friends have already made. This was not the case seven or eight years ago.

Furthermore there are good reasons for believing that the diet of the people most affected has changed in the last seven or eight years. The factors involved in bringing this about are the economic ones which in the last 15 or 20 years have caused a gradual and progressive increase in the cost of food. This increase has been particularly notable in the last seven or eight years as compared to the previous seven or eight years. Again dietary and budgetary investigations have repeatedly shown that there is a very decided difference in the character of the diet of the northern as compared with the southern section of this country. The diet of the South is more largely carbohydrate than that of the North, and with the change in economic conditions, as regards the increased cost of certain foods without a corresponding increase in income, there has naturally and inevitably been a modification of the character of the prevailing diet tending toward a further increase in the carbohydrate component and a reduction in the more costly animal protein elements. The effect of such influences will naturally be most apparent in that locality where the prevailing type of diet already has the narrowest margin of safety. Such are some of the more important factors which must be considered in explaining the alleged increased prevalence of recent years.

Another point mentioned by Dr. Siler was that he had observed that in spite of the fact that a good diet was given pellagra patients, even apparently mild cases, some nevertheless died in a month or six weeks. I quite agree that this may happen, although rarely; but I can not quite see how that affects the question before us. We have the same thing in beriberi and scurvy.

Then the point was raised that in spite of the fact that individuals go back to their old diet they do not always develop pellagra again. The fact that people go back to what apparently was their diet before their attack does not constitute conclusive evidence that the diet is in fact exactly as it was before their attack. Such statements take cognizance of superficial appearances only. They do not and can not recognize apparently slight differences which may

in reality make all the difference between an inadequate and an adequate diet. It is a type of argument that I am sorry to say is altogether too frequent. It deals simply with surface indications.

With regard to the marked difference in sex incidence in individuals with the same diet available, it is well to recall that a difference in sex incidence under like circumstances is recorded for both scurvy and beriberi, only that in these the preponderance of cases is in the male, not in the female. It would seem therefore that we are dealing here with a difference in physiological requirement in the two sexes, an interpretation that is by no means without experimental evidence for its support. Other factors probably also contribute to the bringing about of this difference in sex incidence.

The CHAIRMAN. We will now have to pass to the next paper, entitled "The known and the unknown with regard to the etiology and prevention of beriberi," by Capt. Vedder.

THE KNOWN AND THE UNKNOWN WITH REGARD TO THE ETIOLOGY AND PREVENTION OF BERIBERI.

By EDWARD B. VEDDER,

Captain, Medical Corps, United States Army.

There are certainly few diseases concerning which we are in a position to state that everything with regard to them is known. While in general, sanitary measures adopted to prevent a given disease must be based upon accurate knowledge of the cause and methods of transmission of that disease if they are to be effective, yet very effective sanitary work in the past has been based upon information which while accurate is still incomplete. The sanitarian has controlled smallpox by vaccination in spite of the fact that no satisfactory demonstration has yet been made with regard to the exact biological relationship between vaccinia and smallpox. Yellow fever has been eradicated in several localities by a warfare against the transmitting agent, the stegomyia mosquito, although the etiologic agent of the disease is still unknown.

It may be worth while to take stock of our knowledge concerning beriberi. Do we know sufficient concerning its etiology to prevent the disease, and what gaps in our knowledge remain to be filled?

Opinions as to the etiology of beriberi have varied widely in the past, but for the most part fall into three categories. Some have believed that it was an infectious disease, some that it was an intoxication, and some that it was caused by a certain deficiency in the dietary of those affected. The result of this confusion has been that with few exceptions the sanitary measures taken to prevent this disease have been futile. It is worthy of note that in the case of these exceptions the measures that succeeded in preventing the disease consisted in certain radical changes in the dietary.

At the present day there is a very general consensus of opinion to the effect that beriberi is caused by a dietary deficiency. It would far exceed the limits imposed upon a paper of this character to go into all the details of the work that has led to this conclusion. Moreover, the writer has elsewhere[1] attempted to sift all this evi-

[1] Beriberi. Wm. Wood & Co. New York, 1913.

dence. As a result of this study, I stated in 1913 that "we are now in a position to prevent beriberi in any community that can and will follow our advice, just as surely as we can prevent smallpox and yellow fever." In a general way this opinion was based on the following facts:

1. The complete failure of the adherents of the infection and intoxication theories to prove their case.

2. The very carefully planned and controlled human feeding experiment of Fraser and Stanton,[1] in which they demonstrated beyond all cavil that beriberi can be experimentally produced in men by too exclusive feeding on overmilled or highly polished rice. This experiment was later repeated by Strong and Crowell [2] in the Philippines with a similar result.

3. The long series of animal experiments which have been repeated with substantially the same results in all parts of the world and by which it has been equally demonstrated that various animals, but particularly birds, when fed on diets that will produce beriberi in man, suffer with a disease which in some instances is identical in symptomatology and pathology with human beriberi and in other instances is so similar that we must believe that it is essentially the same disease.

4. The instances referred to above in which beriberi has been eradicated from various institutions or groups of men by certain simple but radical changes in the dietary. Every sanitarian should be familiar with the practical results of this character reported by Van Leent,[3] Vorderman,[4] Takaki,[5] Fletcher,[6] Highet,[7] Heiser,[8] Theze,[9] Chamberlain,[10] and others.

However, beriberi has still continued to prevail in many localities, chiefly because sanitary officers have not been convinced of the truth of the statement that beriberi is a deficiency disease and have been unwilling to adopt the necessary dietary changes. Since 1913, when the writer published the results of his investigation,[11] there has been a considerable amount of experimental work that has confirmed the belief that beriberi is caused by a dietary deficiency, and not one iota of evidence to the contrary that will stand careful analysis. Many statements casting doubt on the dietary origin of beriberi have appeared during this time in the literature. These instances will not bear careful investigation. Most of them consist of occasions in which beriberi is reported to have occurred in spite of the fact that the dietary is stated to have been "satisfactory as to quantity and quality." In all of these cases either no details at all or entirely insufficient data as to the diet actually eaten are given. Often these epidemics are reported by the very man responsible for the diet used, and who would naturally believe that it was satisfactory, although he might actually have very small reason for this belief. After having analyzed a number of such instances the writer stated, in 1914,[12] that "it will not be sufficient in the future, in attempting to disprove the dietary origin of beriberi, to make statements that the diet was liberal and varied.

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[1] Studies from the Institute for Medical Research, Federated Malay States, 1909, No. 10.

[2] The Etiology of Beriberi. Philippine Journ. Science, 1912, VII, 271.

[3] Arch de Med. Nav. 1867, Oct., p. 241. Communication sur le Beriberi, Cong. Internat. d. Sc. Med. Amst. 1880, VI, 170, etc.

[4] Onderzoek naar het verband tusschen den aard der rystvoeding in de gevangenissen op Java en Madoera en het voorkomen van beriberi onder de geinterneeden. Batavia, 1897.

[5] Three Lectures on the Preservation of Health Amongst the Personnel of the Japanese Navy and Army. Lancet, 1906, I, 1369, 1451, 1520, etc.

[6] Rice and Beriberi. Journ. Trop. Med. and Hyg. 1909, XII, 127. Lancet 1907, I, 1776, etc.

[7] Beriberi in Siam. Philippine Journ. Science 1910, V, 73.

[8] Practical Experiences with Beriberi and Unpolished Rice. Philippine Jour. Science 1911, VI, 1237. Also Journ. Am. Med. Ass. 1911, LVI, 1238.

[9] Note sur le Beriberi a Poulo-Condore. Ann. d'Hygiène de Med. Col. 1910, XIII, 16.

[10] The Eradication of Beriberi from the Philippine Scouts by means of a Simple Change in their Dietary. Philippine Journ. Science, 1911, VI, 133.

[11] Beriberi, Wm. Wood & Co., New York, 1913.

[12] Some Further Remarks on Beriberi. Am. Journ. Tropical Diseases and Preventive Med. 1914, I, 826.

Any such communication to be worthy of attention should contain a detailed statement of the food actually consumed by the affected persons, for the 90 days prior to the development of the disease, showing components, quantities, and a statement as to whether the articles used were fresh, canned, or otherwise preserved."

Therefore, while we do not even suggest that our knowledge concerning beriberi is complete, it is believed that the points that remain for investigation are of scientific rather than of practical interest. They concern the chemist, the physiologist, and the clinician and need give no concern to the practical sanitarian, who can eradicate beriberi by compelling the use of a proper diet, even though the exact physiological action of the vitamines has not yet been determined. I would even go further and say that the sanitarian who is faced by a widespread occurrence of beriberi and refuses to recommend the changes in the diet that experience has proved will prevent beriberi is in the same class with the man who to-day would disinfect the mails to prevent yellow fever.

There are however many misconceptions concerning beriberi and deficiency diseases in general which should be dissipated. Many suppose that beriberi only occurs on a diet of rice. Beriberi is a disease resulting from faulty metabolism and is directly caused by the deficiency of certain chemical substances in the food. These chemical substances have been called vitamines. Certain foodstuffs have been shown to be either relatively or absolutely deficient in these beriberi-preventing vitamines, while other foodstuffs contain a rich supply. If a group of men live almost exclusively upon those foods that are deficient in beriberi-preventing vitamines, beriberi will almost surely develop. The danger of contracting beriberi is therefore greatly increased by the consumption of a poorly-balanced or one-sided dietary. Beriberi may occur, however, on a mixed diet furnishing a sufficient number of calories and containing the proper ratio of fats, proteids, carbohydrates, and salts, if all of the articles of this ration are deficient in the vitamines that prevent beriberi. Such occasions are infrequent, but they occur often enough to cast doubt upon the fact that beriberi is a deficiency disease in the minds of those who are not fully acquainted with the evidence that incriminates certain foods.

Obviously the sanitarian should know which foods have been proved to be beriberi producers and which foods will correct this deficiency. The rôle played by polished or overmilled rice, or rice that has been denuded of its aleurone layer, in the production of beriberi is too well known to deserve more than a passing comment. The fact that the great endemic centers of beriberi are almost always confined to peoples that use rice as the staple article of diet is a sufficient commentary on the part played by rice in the production of beriberi.

It does not appear to be so generally known that various carbohydrate foods, such as tapioca, sago, and the various starches and sugars are quite as deficient in vitamines as rice and will produce beriberi in man or animals with great certainty when used too exclusively as articles of diet. It is even more important to note that ordinary white wheat flour is also very deficient in vitamines. Little [1] was perhaps the first to report the occurrence of beriberi among men living almost exclusively on fine wheat flour. but the literature is full of outbreaks of what was evidently beriberi in jails, asylums, and other institutions where bread has been used as the main staple of diet. One of the latest instances of this kind was reported from a jail at Elizabeth, N. J., by Parker.[2] It has also been shown [3 4] that fowls fed upon a combination of rice and bread, or upon bread alone, develop polyneuritis quite as promptly as when fed exclusively upon rice. All food products made of white-wheat flour must be regarded

[1] Beriberi caused by Fine White Flour. Journ Am. Med. Ass. 1912, LVIII, 2 2029.

[2] A Report on Beriberi in the County Jail at Elizabeth, N. J. Pub. Health Reports, 1914, XXIX, 339. See also Vedder, Some Further Remarks on Beriberi. (Reference 12.)

[3] Vedder and Clark. Polyneuritis Gallinarum, a Fifth Contribution to the Etiology of Beriberi. Philippine Journ. Science, 1912, VII.

as deficient in beriberi vitamines and as beriberi producers. Macaroni falls into this category. It produces polyneuritis in fowls,[1] and on at least one occasion [2] a sanitary officer endeavored to prevent the occurrence of beriberi by substituting macaroni for the rice previously used. Quite as much beriberi occurred after this change as before, and in this particular case, instead of concluding that both foods were deficient, the erroneous deduction was made that the disease was not of dietary origin.

It should also be noted that all canned foods must be regarded as possible beriberi producers. It has been shown by numerous investigators, including the writer,[3] that heating to 120° C. destroys the beriberi preventing vitamines in certain foods. All protein foods that are canned must be subjected to about this amount of heat in order to kill all the putrefactive organisms, and such canned foods are undoubtedly beriberi producers when used in excess. I have seen at least one case of undoubted beriberi in a white man, a ship's officer, who had eaten a most varied and satisfactory diet except that for the previous four months everything he had eaten had been canned.

Corn meal and potatoes are intermediate foods. The evidence from experimental animals seems to indicate that beriberi has been occasionally produced by feeding these foods. No extensive occurrence of human beriberi to be attributed to these foods is known to exist. It is certain however that they are relatively deficient in protective vitamines because their curative or prophylactic value in animals or men fed on rice is practically nil. They can not therefore be used to balance an otherwise deficient ration.

On the other hand a number of foodstuffs have been found to be relatively very rich in beriberi preventing vitamines. This is particularly true of rice polishings or the powdered aleurone layer removed from the rice in the process of milling. Rice which has been undermilled and which therefore retains the major portion of the aleurone layer, has been definitely proven to prevent the occurrence of beriberi. However, in the introduction of such rice as a prophylactic, three difficulties have been encountered. One that it is difficult to keep the rice up to specifications. This can be guarded against by examining a sample of every lot of rice delivered. If a few grains are stained by Gram's iodine solution, the percentage of the aleurone and pericarp remaining can be determined in an instant. Secondly, this rice is difficult to keep as weevils and other insects are very apt to infest it if it is kept long. The authorities of Java,[4] have investigated several preservatives, and have found that the preservation of undermilled rice may be secured by placing here and there among the rice, bottles or tins containing chloroform or carbon tetrachloride CCl_4. They state that the use of these chemicals is without a single disadvantage, and that they do not influence the taste or smell of the rice or affect its prophylactic value. The third objection to the use of undermilled rice is that natives that have been accustomed to the use of polished rice will frequently refuse to eat undermilled rice. For this reason, although the use of undermilled rice has been made compulsory among the native troops of the Army (Philippine Scouts) and in all civil institutions in the Philippines, there is no means at present of compelling the native population to use it. For this reason, a tax on overmilled or polished rice has been advocated,[5] of such an amount as to practically render such rice prohibitive in price for the poor people who are the

[1] Wellman and Bass. Polyneuritis Gallinarum Caused by Different Foodstuffs, etc. Am. Journ. Trop. Dis. and Preventive Med. 1913, I, 129.

[2] Lovelace. Peripheral Neuritis in the Amazon Valley. Am. Journ. Trop. Dis. and Prev. Med. 1913, I, 140. See also Journ. A. M. A. 1912, LIX, 2134.

[3] A Fourth Contribution to the Etiology of Beriberi. Philippine Journ. Science, 1912, VII, 419.

[4] Ottow. Testing, Storage, and Preparation of Unpolished Rice. Natuurkundig Tyjdschrift voor Ned. Indie. 1915, LXXIV, 143.

[5] Heiser. Beriberi: Governmental aid in its Eradication. Medical Record, 1912, LXXXI, 516. Vedder. The Prevention of Beriberi. Transactions 15 Internat. Cong. on Hyg. and Demography. See also Beriberi, Wm. Wood & Co., 1913.

main sufferers from beriberi. This would compel these people to use undermilled rice which can be sold at a cheaper rate than polished rice and which in addition would prevent beriberi.

It has also been ascertained that various species of legumes, such as ordinary white beans, and several varieties of peas when added to a ration of polished rice, will prevent the occurrence of beriberi.[1] It has also been shown experimentally,[2] that peanuts will prevent avian polyneuritis. It is probable that all leguminous vegetables are rich in beriberi preventing vitamines.

The Japanese have found that barley is an efficient prophylactic against beriberi.[3] Barley also prevents the development of polyneuritis in birds fed on polished rice.

There are undoubtedly other foods than the ones mentioned which when used too exclusively may produce beriberi. There are also undoubtedly other foods that possess a prophylactic value. It would be of some practical value if all foodstuffs were tested esperimentally to determine their content in beriberi preventing vitamines, and the writer hopes some day to carry on this work. In the meantime, however, as already stated, the sanitarian may at any time eradicate beriberi by substituting for some of the beriberi producing foods enumerated above, either undermilled rice, beans, or barley, or preferably a combination of these foods. The combination is preferable when possible, because through accident or design some of the people whom we aim to benefit may fail to eat one of the above prophylactics, and this danger is reduced to a minimum if several such prophylactics are used.

Passing to the unknown with regard to beriberi there are three problems that are of the utmost scientific interest. These may be stated as follows: 1. The relationship between dry and wet beriberi. Are these two types of the disease caused by the deficiency of the same vitamine or by different vitamines? 2. What is the physiological action of the vitamines? Do they act as indispensable building stones for certain tissues, or are they concerned in some other manner, as, for instance, in carbohydrate metabolism? 3. What is the chemistry of the vitamines? The solution of these problems is not only of great importance to a proper understanding of beriberi, but will probably throw much light upon other deficiency diseases and upon our conceptions of physiological problems.

1. *The relationship between dry and wet beriberi.*—Although the paralytic symptoms in beriberi may be easily explained as a result of the degenerations that occur in the nervous system, no rational explanation of the occurrence of the anasarca and effusions that characterize wet beriberi has been afforded. If the pathological condition known as dry beriberi and that known as wet beriberi are both produced as the result of a deficiency of one vitamine, what is the explanation of the well-known fact that in one epidemic most of the cases will be of the dry type, while in another epidemic most of the cases will be of the wet type?

I have thought,[4 5], that a probable explanation of this strange phenomenon is afforded by the theory that dry beriberi is caused by the deficiency of one vitamine, while wet beriberi is caused by the deficiency of another vitamine. There is a certain amount of experimental evidence in favor of this theory, since it has been found that a simple alcoholic extract of rice polishings contains substances that will produce an immediate cure in cases of wet beriberi, while it is entirely ineffective in the treatment of dry beriberi. However if the rice polishings are treated in a different manner, the vitamine that cures dry beriberi is obtained, and its administration results in a prompt

[1] Hulshoff Pol. Katjang-idjo, un nouveau medicament contre le Beriberi. Janus 1902, VII, 524, 570 See also Beihefte Zum Arch. f. Schiffs u. Tropenhyg. 1910, XIV, 7.

[2] Rommel and Vedder. Beriberi and Cottonseed Poisoning in Pigs. Journ. of Agricultural Research Dept. of Agriculture, Wash., D. C., 1915, V, No11, 488.

[3] Saneyoshi. On Kakke. Proceedings of the XIII Internat. Congress, Paris, 1900, XVII, 78.

[4] Vedder. Beriberi, Wm. Wood & co, New York, 1913.

[5] Vedder and Clark. Polyneuritis and Gallinarum, a fifth contribution to the Etiology of Beriberi. Philippine Journ. Science, 1912, VII.

cure of the paralytic symptoms of dry beriberi. These facts at least indicate the possibility that rice polishings contain two distinct though probably chemically related vitamines. Unfortunately conclusive evidence as to the truth or falsity of this theory has not yet been obtained because a suitable experimental animal has been lacking. Fowls and pigeons are ideal experimental animals for the production of dry beriberi but appear to suffer rarely, if at all, from wet beriberi, and typical wet beriberi can not be produced with any degree of regularity in any of the common laboratory animals. However, within the past year Rommel and Vedder,[1] have found that pigs fed on polished rice suffer from wet beriberi in a considerable percentage of cases. Further work is now in progress, and it is to be hoped that, having found a suitable experimental animal, an explanation of the relation between dry and wet beriberi may soon be afforded.

2. *What is the physiological action of the vitamines.*—I have been strongly of the opinion that the vitamine of dry beriberi is a building stone which is essential for the metabolism of the nervous tissues. This opinion is based upon the following facts:

1. If the supply of this vitamine is cut down by feeding exclusively on polished rice, changes in the structure of the nerve fibres of fowls may be demonstrated after only 7 days on such a diet. The evidence of beginning degeneration at such an early date appears to indicate that a certain amount of this vitamine is constantly necessary in order to maintain the nervous system in a healthy condition.

2. The nerve cells from the cord of fowls suffering from polyneuritis gallinarum present changes very similar to those demonstrated in the nerve cells of birds that suffer from fatigue as the result of long flights.

3. Fowls suffering from polyneuritis may be completely cured within a few hours by the administration of the vitamine obtained from rice polishings.

This evidence at least strongly suggests that this vitamine is a constituent that is essential to the normal metabolism of nervous tissue. It is difficult to understand how it can act in any other manner than as a building stone of that tissue.

More recently Funk,[2] and Braddon and Cooper,[3] found that when fowls were allowed a fixed amount of vitamine, the greater the proportion of carbohydrate in the food, the quicker was the onset of polyneuritis. From this evidence these investigators conclude that the vitamines play an active rôle in the assimilation and metabolism of carbohydrates, and that it is in this way rather than as a building stone for nervous tissues that vitamines are essential to the life of the organism.

It appears to me that this conclusion is premature to say the least. It has always been supposed that carbohydrate foods were chiefly of value in the animal economy as fuel, or as a source of heat and energy, rather than as tissue builders. It seems highly improbable that carbohydrates are of such importance in the metabolism of the nervous tissue, that a fault in carbohydrate metabolism would result in the profound degeneration of the nervous system seen in beriberi. But aside from such a priori reasoning, there is experimental evidence which it is difficult to reconcile with such a theory. Schaumann,[4] produced paralysis with evidence of degeneration in the nerves, in both rats and dogs by feeding them exclusively on meat that had been sterilized in an autoclave at 120° C. If beriberi and nerve degenerations may be produced as the result of the destruction of the vitamines in animals that eat no carbohydrate food, this would appear to show that the vitamines are essential to the body in some other way than as factor in carbohydrate metabolism.

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[1] Beriberi and Cottonseed Poisoning in Pigs. Jour. of Agricultural Research, Wash., D. C., 1915, V, Noll. 488.

[2] Funk. Die Rolle der Vitamine beim Kohlenhydrat-Stoffwechsel. Roppe-Seylers Zeitschrift fur Physiologische Chemie 1914, LXXXIX 378.

[3] Braddon and Cooper. The Influence of Metabolic Factors in Beriberi. Journ. of Hygiene 1914, XIV, 331. See also Brit. Med. Journ. 1914, I, 1346.

[4] Schaumann. Die Aetiologie der Beriberi unter Berucksichtigung des Gesamten Phosphorstoffwechsels. Beiuefte. zum Arch. f. Schiffs u. Tropenhyg. 1910, XIV, 335.

Funk [1] performed one experiment in an endeavor to show that beriberi is not an intoxication, difficult to reconcile with the theory that the vitamine is concerned in carbohydrate metabolism. Four healthy doves and four doves in the last stages of polyneuritis were killed, plucked, and finely minced and extracted with three times their volume of absolute alcohol in a shaking machine. The extracts were filtered and evaporated in vacuo. The residues were taken up with water and fed by mouth to birds suffering from polyneuritis. In all eight cases a cure was effected, with the extract from birds suffering from polyneuritis, as well as with the extract from normal birds. This contradicts the intoxication theory, since no trace of intoxication resulted from the administration of extracts of birds suffering from polyneuritis, but on the contrary a cure. The extract from healthy birds contained more vitamine. Funk says: "This experiment shows that all the vitamines of an organism can not be mobilized to take part in metabolism. It appears also that the organs most essential to life are the ones first robbed and the animal dies before the whole supply of vitamine is exhausted from the body." It appears to me that Funk here admits what he elsewhere denies, namely, that the vitamines exist in the body as constituents of the tissues and particularly of nervous tissue.

Further experiments are greatly needed to determine the exact rôle of the vitamines in the metabolism of the body. But at present I see no reason to doubt that one of them is concerned in some way with the metabolism of nervous tissue, probably as a building stone, and that this is the most plausible explanation of the degeneration of the nervous system in beriberi, which occurs when this vitamine is withdrawn.

What is the chemistry of the vitamines?—The study of the chemistry of the vitamines has been a source of confusion. Funk [2] claimed to have obtained the viatmine from rice polishings in a pure state and gave its empirical formula. Edie [3] and his coworkers obtained a different formula. Suzuki and Shimamura and Odake [4] by a different method obtained a vitamine of still different chemical composition. Vedder and Williams [5] obtained substances that would promptly cure fowls suffering from polyneuritis, but were not able to obtain sufficient vitamine in a pure state to submit it to chemical analysis. Finally, Drummond and Funk [6] now admit that they can not isolate the pure vitamine and say that it is apparenly decomposed during the fractionation, and all trace of it is lost. The chemist who reads these various papers might come to the conclusion that the very existence of such a thing as vitamine was doubtful. However the fact that a vitamine exists is as well proven as any natural fact can be.

All of the above investigators have succeeded in obtaining from rice polishings a chemical substance, which in doses of a few milligrams was capable of curing birds suffering with polyneuritis induced by a diet of overmilled rice. The explanation of the uniform failure to obtain a sufficient amount of this substance in the pure state for a satisfactory chemical analysis is very simple. In various foodstuffs it is a very minor quantitative constituent and it is very difficult to extract. It is rapidly destroyed by most of the chemical reagents that are used to fractionate these complex foodstuffs and is a most unstable body even when minute quantities are obtained.

Mr. Williams who worked on the chemistry of the rice polishings in Manila has been able to continue this work and is now able to make some definite suggestions with regard

[1] Experimentelle Boweise gegen die toxische Theorie der Beriberi. Hoppe-Seylers Zeitschrift f. Physiologische Chemie. 1914, LXXXIX, 373.

[2] On the Chemical nature of the Substance which cures Polyneuritis in Birds. Journ. Physiology, 1911, XLIII, 26 also 1912, XLV, 75.

[3] Edie, Evans, Moore, Simpson, and Webster. The Anti-Neuritic bases of Vegetable origin with a Method of Isolating Torulin. Bio-Chem. Journ. Liverpool, 1911-1912, VII, 234.

[4] Ueber Oryzanin, etc. Biochemische Zeitschrift, 1912, XLIII, 89.

[5] Concerning the Beriberi Preventing Substances or Vitamines contained in Rice Polishings. Philippine Journ. Sc. 1913, VIII, 175.

[6] The Chemical Investigation of the Phospho-Tungstate Precipitate from Rice Polishings. Biochemical Journal, 1914, VIII, No. 6, 598.

to the chemical constitution of the beriberi vitamine and the reason for its unstable nature.

We thus find that while there are still important problems connected with beriberi they are all being studied and there is a fair prospect that they will be solved.

In closing I can not refrain from commenting on the attitude of several physiologists toward the new conception of the vitamines and toward the term itself. Thus one physiologist who has several times objected to the use of the term vitamine says in a recent paper:

> I am conscious, in the midst of our enthusiasm, of a warning given by Rubner in a protest against the creation of a new scientific vocabulary and the danger of transforming the natural sciences into a play of words. The science of nutrition must never tolerate the substitution of unhealthy speculation for what is admittedly a laborious undertaking, namely, experimentation.

The conception of the vitamine rests securely upon experimental evidence. I suppose there was a time when Harvey's discovery of the circulation of the blood was termed a "play of words" and "unhealthy speculation" by some of the scientific "standpatters" of that day. The chemical constitution of the vitamines has been very uncertain although there is good reason to believe that the beriberi vitamines are members of the pyrimidine group. But if the chemistry of these bodies should never be thoroughly understood, it is equally true that the chemistry of our common foods, of our secretions, and even of the blood itself is still very obscure.

With regard to the term itself it may be possible later to find a better one. But in the meantime we are obliged to name this substance before we can discuss it. "No ideas can materialize except through their expression," and for the present the term vitamine is quite as useful and plays the same rôle in our scientific vocabulary as the terms enzyme, hormone, and antibody. The existence of these substances has been demonstrated by experimentation, and we can not ignore them because we are as yet ignorant concerning their chemistry.

The CHAIRMAN. There are two other papers on this subject. If there is no objection, we will defer the discussion until after the completion of these papers. We will now have the paper of Dr. Lebredo, of Cuba.

BERIBERI, ESTUDIO EPIDEMIOLÓGICO Y EXPERIMENTAL

Por MARIO G. LEBREDO,

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De ninguna manera negaremos que el arrez pulimentado, cuando se administra en grandes cantidades, como alimento principal o exclusivo, a diversos animlaes en los estudios experimentales, provoca verdaderos trastornos de origen polineurítico.

Igualmente está plenamente demostrado, que esas polineuritis experimentales, se deben, en definitiva, a la pobreza que en principios fosforados tiene el arroz pulimentado, principios nutritivos importantes que quedan en el desecho del arroz en las operaciones de pulimentación.

Por lo tanto, es evidente que, en los países donde el arroz es alimento principal o exclusivo, han de encontrarse, naturalmente casos de esas formas polineuríticas, análogas a las experimentalmente provocadas en animales y clasificadas como beriberi.

Pero, punto concreto que hemos de abordar: ¿Debe de quedar aceptada de manera definitiva, como única, esa explicación etiológica? ¿Deberá quedar convenido que

es sólo una enfermedad producida por falta de principios nutritivos, determinados, en el arroz y que, por lo tanto, sea asunto resuelto que ocupe el beriberi en los futuros congresos el lugar principal que ocupa en éste entre las enfermedades producidas por una alimentación deficiente (starvation).

Nosotros creemos que hay algo más que hacer; creemos que, también, debe de haber algo activo que produzca el beriberi.

Y lo creemos porque, no siempre, reviste la forma crónica, la depauperante, perfectamente explicable por prolongada carencia de determinado principio nutritivo; porque no todos los que utilizan el arroz como alimento exclusivo se hacen beribéricos, como debiera suceder, indefectiblemente, de ser la carencia del elemento nutritivo indispensable, el causante de esa enfermedad. Por el contrario, unas veces formas agudas sorprenden a individuos que hasta entonces gozaron de perfecta salud y que comían el arroz agregado a una variada alimentación; y otras veces, formas verdaderamente fulminantes, se presentan, también, en individuos que, durante años, han estado sometidos—sin presentar la menor manifestación patológica—a la exclusiva alimentación del arroz, ataques fulminantes que estallan de repente, como si algún elemento patógeno hubiera venido a provocarlos.

Nos parece que sería lógico aceptar—y conveniente diferenciar con nombres adecuados, dos mecanismos etiológicos: uno, el puramente alimenticio, provocando polineuritis a tipo crónico y la predisposición; otro, el tóxico, también orizeo, provocador de fenómenos de intoxicación aguda y subaguda y, quizás, crónica del genuino beriberi.

I. En el trabajo que vamos a someter a la consideración de ustedes, exponemos algunos hechos interesantes de epidemiología del beriberi en Cuba, en relación con un estudio especial de virulencia de los arroces consumidos en y fuera de los lugares donde se presentó la enfermedad.

Nada hay más provechoso para el investigador, que el estudio de las epidemias, en regiones indemnes, de aquellas enfermedades que existen, constituyendo focos endémicos, en determinados países. Y mayor provecho hay si ha sido necesario llevarlo a cabo desde el importante punto de vista sanitario.

En los focos endémicos, por lo general, el interés sanitario es de disminución y, por lo tanto, no llegan a discernirse bien los matices de los casos benignos que en epidemiología son tan graves. Experiencia de ello, y grande, tuvimos con la fiebre amarilla, enfermedad que vino a mostrar bien sus formas atenuadas, benignas, cuando la acción sanitaria, enérgica, hizo descender la secular endemia amarilla, a reducidos límites epidémicos.

Con el beriberi pasó lo mismo.

En Cuba se tuvo al beriberi como enfermedad corriente, abundante, casi endémica, en las plantaciones de azúcar, en la época de la esclavitud, época en que la inmigración de esclavos africanos y hasta de semi-esclavos chinos, parecía traer, con el contingente propenso a contraer la enfermedad por el duro trabajo y la mala alimentación a que se les sometía, la causa desconocida de la enfermedad, naturalmente considerada exótica.

En un trabajo que publicamos[1] en 1913 expusimos, que, en esa época y las siguientes hasta la de nuestra independencia, no fueron diagnosticados beribéricos todos los que debieron serlo, pues se pasaban por alto los casos fugaces, ni fueron positivos todos los diagnosticados, engrosando las estadísticas como beribéricos, anémicos palúdicos o a parasitología intestinal, hidrohémicos por miseria, etc.

Sin embargo, encontramos en la literatura médica de ese período, casos aislados y verdaderas epidemias, innegables, de genuino beriberi.

De marzo de 1911 data nuestra primera observación de un interesante brote epidémico bien caracterizado de beriberi.

[1] Beri-Beri. M. G. Lebredo. Boletín Oficial de la Secretaría de Sanidad y Beneficencia de Cuba, mayo y junio de 1913, tomo IX, No. 5 y 6 (en español). En ingles en el tomo X.

Se presentó en los presos de la cárcel de Santa Clara (Provincia de Santa Clara).

Las manifestaciones patológicas fueron muy evidentes y tuvimos oportunidad de hacer la autopsia de un caso, muerto por forma aguda, cuya agonía, dolorosa y cruel, presenciamos.

Deseando hacer un estudio completo del arroz que consumían los atacados, recogimos alguna cantidad, estudio amplio que nos llevó a conclusiones que hicieron arraigar en nosotros la idea, de que el beriberi puede ser producido por un tóxico, desarrollado en el arroz a expensas de la substancia amilácea atacada por un germen amilozimo, tóxico que actúa sobre los elementos nerviosos, estén o no predispuestos.

Las conclusiones provisionales del estudio, fueron presentadas al Congreso de la American Public Health Association, reunido en la Habana el 2 de diciembre de 1911.

La epidemia fué grave: de siete atacados murieron cuatro con fenómenos agudísimos cardio-pulmonares.

Correspondiendo con esa gravedad epidemiológica, el estudio especial del arroz que se consumía allí, mostró una notable virulencia para el curiel.

El arroz contenía un germen amilozimo, a esporos resistentes a la temperatura de 100°C. por más de 20 minutos. Este germen al vivir a expensas de la substancia amilácea del arroz preparado hervido, fabricaba substancias tóxicas (no identificadas), mortales para el curiel, por la vía intra-peritoneal, en dosis de 16 c. c. y aun menos; por la vía cerebral, en dosis pequeñas, gotas; y en un caso, por la vía gástrica, depués de haberse provocado la irritación del aparato digestivo. Las substancias tóxicas parecían tener una exclusiva acción, directa, sobre los elementos nerviosos, irritados o no, ya que fueron inofensivas por las vías subcutánea y circulatoria.

Los fenómenos presentados por el curiel intoxicado mostraron una interesante analogía con los del beriberi agudo, cardio-pulmonar, humano; y en las autopsias encontramos: poca cuagulabilidad de la sangre, dilatación del corazón derecho, exudado en el pericardio, en las pleuras, aun en el peritoneo y más o menos limitada gastro-ileo-yeyunitis, que recuerda la duodenitis que, según Hamilton Wright, acompaña a todo beribérico agudo, o existió en aquellos casos que encontramos ya en época de polineuritis residual beribérica.

II. En junio de 1912, y en febrero y abril de 1913, surge de nuevo la sospecha de estar atacados de beriberi varios penados, en la misma cárcel de Santa Clara donde se presentó la grave epidemia anteriormente citada.

Los casos de junio de 1912 y los de febrero de 1913, no pudieron ser retrospectivamente confirmados. Las historias clínicas de los presentados en abril, señalaron algo más concreto. Fuímos a verlos y no pudimos llegar a conclusiones precisas: ninguno (eran 6), presentaba aspecto clínico que correspondiese a ninguno de los cuadros típicos de las formas intensas del beriberi, ni forma húmeda ni atrófica y menos la terrible forma aguda cardio-pulmonar. En todo caso, si fueron de beriberi genuino, lo fueron de la forma ligera, fugaz.

Creemos que existen esas formas ligerísimas en el verdadero beriberi, tan difíciles de distinguir de algunas manifestaciones polineuríticas de una considerable tenuidad, que pueden manifestarse en los individuos que viven recluídos en los asilos, donde causas de orden moral y, principalmente, el hacinamiento, la vida sedentaria, la posición habitual de pie, la monotonía de la existencia y de la misma alimentación, son suficientes para producirlas.

Ninguna de las muestras de arroz, recogidas en las diversas épocas señaladas, se mostró virulenta para el curiel.

No deja de ser sugestivo el pensamiento de que puedan existir esas formas tenues, no bien acentuadas, fugaces, por acción transitoria del tóxico, cuando el material infectado (arroz) no es muy abundante, coincidiendo la desparación de las invasiones, el poco relieve mostrado por la epidemia y la curación rápida de los invadidos, con el agotamiento del elemento etiológico por consumo del arroz tóxico, resultando entonces tardío el empeño en encontrar muestras infectadas.

III. Arroces de diversas clases y procedencias (canilla viejo [old hard], Valencia corriente, semilla Siam, Valencia Bombay, semilla corriente, canilla nuevo Santiago de Cuba, semilla americano, semilla S. Q.), estudiados en distintas épocas (14 muestras en 1914), no mostraron ningún efecto tóxico sobre los curieles, ni por la vía más activa, la peritoneal, ni en dosis considerable hasta de 20 c. c.

Es cierto que a ocasiones encontramos en estos arroces inofensivos, gérmenes banales a esporos resistentes a 100°C. amilozimos en corto grado, no virulentos; pero estos gérmenes no llegan—o si llegan lo hacen mal—a adoptar la especial forma de tabaco, a reaccion amilodea excepto en el extremo esporulado que en el período de esporulación toma el germen virulento estudiado por nosotros en nuestros arroces tóxicos y el encontrado y aislado por Le Dantec de excrementos de beribéricos.

IV. En diciembre de 1914 se desarrolló en Banes (Provincia de Santiago de Cuba), una epidemia de beriberi, denunciada por el Dr. Ruiz Ariza, médico muy competente, superintendente de la División Banes de la United Fruit Company, quien, solamente en el Hospital de la compañía a su cargo, observó siete atacados.

Ya unos días antes tuvimos noticias de un caso por una historia clínica remitida por el jefe de sanidad de aquella población.

En el año 1908, es decir, próximamente 6 años antes de la época de la aparición de este brote, hubieron varios individuos atacados de beriberi, no sólo en Banes, sino en un embarcadero situado a pocos kilometros de esta población, siendo dos de los casos fatales.

Trasladados a Banes pudimos observar varios casos de genuino beriberi; pero todos, aunque bién pronunciados, ya en período de desaparición sintomática, fin de epidemia. Estudiando retrospectivamente las historias de dos individuos fallecidos al principio de este brote, resulta, que puede considerarse murieran de beriberi agudo, además de otro caso típico (Antonio González) fallecido al día siguiente de haber salido del hospital, con trastornos del corazón, taquicardia, etc., fenómenos gravísimos que, muy amenudo no son sospechados por el mismo enfermo hasta que estallan en crisis mortal.

Según nuestras observaciones, el proceso patógeno desarrollado en Banes, examinado en conjunto fué uno polineurítico, con trastornos más o menos marcados de la motilidad por tensión de los gemelos, con edema tibial, con disminución o abolición total de los reflejos rotulianos, con molestia epigástrica, con pulso frecuente, con angustia precordial, con taquicardia, llegando los trastornos cardio-pulmonares a producir la muerte en los casos enumerados.

Sin entrar en profundas consideraciones con respecto a la sintomatología del beriberi, no podemos menos de señalar que, para nosotros, en todo genuino beribérico—ya se estudie en su primera invasión, o en un brote siguiente—deben de mostrarse, más o menos acentuados, fenómenos cardiacos acompañando a los fenómenos polineuríticos de las extremidades inferiores. A este respecto dice Lacerda con razón: "lo más especial del beriberi es la aparición temprana de los trastornos cardiacos y de los trastornos respiratorios ligados a alteraciones del neumogástrico y del frénico."

En Banes recogimos 16 muestras de arroz, en época en que aun estaban presentes manifestaciones beribéricas en algunos de los casos; de ellas, 7 fueron virulentas para el curiel.

Correspondió a la prueba de virulencia, la presencia de un germen amilozimo semejante al encontrado en el arroz patógeno de Santa Clara, aunque no tan activo en su desarrollo ni en la producción de substancias tóxicas.

V. Ultimamente, en mayo de 1915, llegó a Cienfuegos, procedente de la India, el vapor inglés *Dewa* después de estar en cuarentena por venir de puerto sucio de bubónica (?) atracó al muelle.

Al día siguiente de atracar, ya en operaciones de descarga, murió, repentinamente, el indio Latifallée, de 25 años de edad. Según breve historia recogida, resulta que tuvo al levantarse "un pequeño dolor en la región precordial, a pesar del cual continuó trabajando durante el día; por la tarde se acentuó el dolor acompañado de disnea,

intensa, colapso y muerte." Según el certificado de autopsia, fué diagnosticado de pericarditis.

Tres días después, el médico de puerto visitá el vapor, y encuentra nueve tripulantes con el siguiente cuadro: "aspecto deprimido, flacos, con edema de las extremidades inferiores, cara angustiosa, pupilas contraídas, trastornos de la locomoción en distintos grados hasta notable paraplegia, el reflejo rotuliano en unos notablemente disminuído y en otros abolido, apiréticos, pulso frecuente, ruidos del corazón disminúidos, dolor, en todos, más o menos intenso en la región epigástrica que se irradia a la región precordial." No se pudieron tomar mayores antecedentes epidemiológicos por dificultades de idioma.

Sin embargo, ante el caso de muerte y el cuadro descrito, era lógico pensar que hubo un verdadero brote epidémico de genuino beriberi dentro del vapor *Dewa*.

La alimentación casi exclusiva de la tripulación era el arroz. Interesados por el resultado del estudio de los arroces virulentos y no virulentos, antes mencionados, y por la correlación hallada entre esos resultados y la intensidad de los brotes beribéricos, tenía para nosotros un gran valor el estudio del arroz *Dewa*, que había servido de casi exclusivo alimento a esos individuos de su dotación, atacados de beriberi, en epidemia reciente, con muerte, y en recinto bien limitado.

El arroz recogido resultó particularmente virulento, el más virulento de los estudiados por nosotros, por lo que vamos a dar algunos detalles del trabajo experimental, aprovechando la ocasión para señalar particulares interesantes.

GERMEN.

Contenía un germen amilozimo, a esporo resistente a la temperatura de ebullición por más de 20 minutos, que después del tercer día de germinación adoptaba formas de tabaco, con reacción amiloidea de todo el elemento, excepto en el extremo esporulado.

Este germen resultó, como veremos comprobado después, productor de considerable cantidad de substancias tóxicas (beriberígenas?) para el curiel.

En el arroz preparado, hervido, y dejado con bastante cantidad de agua, 1 : 4, el germen evolucionó. Como es natural, esa evolución influye poderosamente sobre el medio, en el cual se acumulan los productos que se desarrollan al atacar el germen-fermento al almidón del arroz, llegando por concentración de esos productos, después de algunos días, a hacerse impropio para el natural desenvolvimiento biológico del germen. Cuando esto sucede, ocurre polimorfismo por involución.

El germen no se desarrolló bien cuando utilizamos como medio de cultivo otros medios amiláceos, ni cuando esterilizamos el arroz en agua, bajo presión. Su mejor medio de cultivo es el propio arroz que debe esterilizarse seco, en el autoclave y luego, seco y estéril cocido con agua estéril.

Se comprende que cuando el grano de arroz contiene el germen, porque viene naturalmente infectado, y estos son los casos habituales de nuestras pruebas, basta con hervir el arroz, tal como viene, en agua, durante 20 minutos y pasarlo a frasco estéril.

El germen, cultivado en agar, pasó a la forma de resistencia, esporulando, sin dar la evolución morfológica que en el propio cultivo orizeo.

En resumen, el germen del arroz del *Dewa*, en su morfología, biología y reacciones, fué semejante, si no fué el mismo, a los encontrados en los arroces virulentos de las epidemias de Santa Clara y de Banes.

Seguramente que el germen debe de existir, de manera natural, dentro del grano de arroz, infectándose, quizás, en los envasaderos después de pulimentado, y es probable que la corteza (cáscara) y principalmente la película pericárpica, sean contra ello excelentes protectores.

VIRULENCIA.

Este arroz se ha mostrado sumamente virulento.

Via intraperitoneal.—Por vía intraperitoneal ha sido muy mortífero, pues no sólo la cantidad clásica de 16 c. c. del agua del arroz preparado produjo la muerte de los curi-

eles inyectados, sino que cantidades de 10 y hasta de 5 c. c., con sólo 23 ó 24 horas de preparado el arroz, mataron a los curieles, en 1½, 5, 6 y 9 horas.

Dosis de 1 c. c. nada produjeron.

Inyección intraperitoneal.

Curiel.	Fecha.	Cantidad.	Tiempo preparado el arroz.	Tiempo muerte después inyección.	Fenómenos y autopsia.
		c. c.	*Horas.*	*Horas.*	
No. 1	Mayo 26	16	23	1 a 1½	Típicos.
No. 1, 2 S	Junio 18	16	24	6 a 7	Do.
No. 2, 2 S	...do	10	24	8 a 9	Do
No. 3, 2 S	...do	10	24	5	Do
No. 4, 2 S	...do	5	24	24	Do.
No. 10, 2 S	Julio 20	1	[1] 5	No.	No.
No. 11, 2 S	...do	1	[1] 5	No.	No.

[1] Días.

Los fenómenos tóxicos fueron los mismos que los provocados por los arroces tóxicos de Santa Clara y Banes. A veces hay, inmediatamente después de hecha la inyección, ligeros fenómenos de shock, manifestados por alguna inquietud y sobresaltos, pero son fenómenos que duran muy poco tiempo.

Los propios síntomas tóxicos no aparecen, nunca, antes de la media hora de haber sido inyectados, y se suceden de la siguiente manera: ligero malestar que se acentúa rápidamente, lenta progresiva angustia, respiración con contragolpe diafragmático, que poco a poco se hace más dificultosa, erizamiento del pelo del cuello y cara, posición recogida en bola, y a veces con aspecto leonino, ojos hundidos, sufrimiento, martilleo de la cabeza con movimientos isócronos con los golpes diafragmáticos, caída de lado, agonía lenta, y muerte, conjunto sintomático que corresponde según parece deducirse de la autopsia, a trastornos cardio-pulmonares. No ha habido retensión de orina, ni parálisis intestinal.

En la autopsia encontramos: exudado en las pleuras, en cantidades de 0.1, 0.2, 0.25, 0.4 hasta 1.5 c. c.; exudado en el pericardio, en cantidades de 0.1, 0.2, 0.3 c. c.

Exudado.

Curiel.	Cavidades pleurales.		Pericardio.
	Derecha.	Izquierda.	
	C. c.	*C. c.*	*C. c.*
No. 1, 1 a S	0.1	1.5	0.1
No. 1, 2 a S	1.5	.25	.2
No. 2, 2 a S	.0	.0	.2
No. 3, 2 a S	.4	.1	.2
No. 4, 2 a S	.2	.1	.3

No transcribimos el resultado de la medición del líquido encontrado en el peritoneo, porque como la inyección ha sido hecha por esta vía, no ha habido tiempo, por muerte rápida, a la total absorción del líquido inyectado. Esa medición es importante en los experimentados por la vía subdural y gástrica.

Los demás caracteres de autopsia fueron los habituales hallados en las experiencias con los arroces de Santa Clara y Banes: dilatación del corazón derecho, siempre en más o menos amplitud, y algunas veces de la aurícula izquierda muy ingurgitada; venas cavas y sus gruesos afluentes, principalmente los de la superior, sumamente ingurgitadas, encontrándose un verdadero molde de esos vasos, en gran parte de su trayecto, hasta el corazón, formado por la sangre coagulada, cuando la autopsia es

tardía; cuando es muy reciente la muerte hay que ser muy cuidadosos para esa observación de plenitud vascular venosa, pues es considerable la disminución de la coagulabilidad sanguínea; color del corazón, pardo obscuro, con gran congestión de sus paredes, y ocasional equímosis pequeño; diafragma la mayor parte de las veces muy abovedado, reduciendo considerablemente el espacio de la cavidad toráxica; pulmones, a veces muy blancos, pálidos, con focos bien determinados de infartos hemorrágicos, y, al corte, como enfisematosos, otras veces, más congestionados; intestino delgado, principalmente yeyuno, e íleon, color rojo, hasta rojo vinoso, y el estómago con algunas zonas congestivas que llegan en algunos casos el grado de equímosis.

Via intracraneana.—Ha sido menos mortífera que la intraperitoneal. Los curieles murieron en 4½, 8 y 9 horas después de la inyección, desde gotas hasta 0.1 c. c. del agua de arroz virulento, de 43 horas a 8 días de preparado.

Inyección intracraneana.

Curiel.	Cantidad.	Tiempo preparado el arros.	Tiempo muerte después inyección.	Fenómenos y autopsia.
No. 2, 1 a 8	VI gotas	43 horas	9 horas	Típicos.
No. 2, 1 a 8	...do	...do	...do	Do.
No. 4, 1 a 8	0.1 c. c	6 días	No	No.
No. 4, 1 a 8	.1 c. c	8 días	...do	Do.
No. 6, 1 a 8	.2 c. c	8 días	...do	Do.
No. 6, 1 a 8	.2 c. c	8 días	7½ horas	Típicos.
No. 5, 2 a 8	.2 c. c	5 días	No	No.
No. 6, 2 a 8	.1 c. c	5 días	...do	Do.
No. 7, 2 a 8	.2 c. c	5 días	15 horas	Típicos.

En total: de 7 inyectados, murieron 4 solamente.

La técnica de la inyección es simple: punción ósea, punción delicada de las membranas cerebrales con una aguja de disección fina, penetrando muy ligeramente en la substancia cerebral, de manera que se provoque una ligera irritación de la víscera, sin grave traumatismo. La inyección del agua de arroz virulento preparado, se hace muy cuidadosamente, sin hacer presión sobre la delicada estructura cerebral. Quizás algunos de los fracasos experimentales por esta vía, se deban a un exceso de precaución de este particular de la técnica.

Cuando, a pesar de todo cuidado, se ha producido un traumatismo grave, se presentan, inmediatamente después de la inyección, contracturas fuertes hacia uno u otro lado, hasta convulsiones, en cuyo caso desechamos al animal en experimentación. Si solamente se presentan ligerísimos movimientos de inquietud, de torsión hacia uno u otro lado, rápidamente fugaces, se deben al "shock."

Los fenómenos tóxicos, se presentaron a la media hora de la inyección.

Los síntomas fueron: inquietud, marcha algo parética con ligero titubeo de las extremidades posteriores; luego, inmovilización, sin parálisis, con gran malestar mientras se establecen los trastornos respiratorios con notables movimientos de contragolpe diafragmático; después se echan de lado, erizamiento, etc.; los trastornos cardio-pulmonares se hacen más graves, y agonizan con relativa lentitud.

Nunca, en ninguno de los casos, (por ninguna de las tres vías efectivas para el tóxico), ha habido retención de orina, ni parálisis intestinal. Al contrario, la orina, abundante, se elimina con fuerza, siendo también muy notable el aumento del peristaltismo intestinal. La orina, examinada mucha veces, no ha mostrado sino ocasional traza de albúmina.

En la autopsia encontramos: exudado pericárdico 0.1, 0.2 y 0.25 c. c.; y, hecho muy notable, exudado peritoneal en cantidad de 2, 3 y 5 c. c. Todos estos exudados perfectamente límpidos, transparentes.

Exudado.

Curiel.	Cavidades pleurales.		Pericardio.	Peritoneo.
	Derecha.	Izquierda.		
	C. c.	*C. c.*	*C. c.*	*C. c.*
No. 2, 1 a S	0.0	0.0	0.25	5.0
No. 2, 1 a S	.4	.0	.2	2.5
No. 6, 1 a S	.0	.0	.1	3.0
No. 7, 2 a S	.1	.1	.2	5.0

Por lo demás, iguales manifestaciones viscerales que por las otras vías, aunqe mucho más ligera la congestión del intestino delgado y de los mesenterios correspondientes.

Nada se encuentra en la cavidad craneal; si acaso, el sitio de la inoculación señalado por un punto casi imperceptible; pero, por lo demás, no hay apreciable congestión ni reblandecimiento de las superficies cerebrales.

Vía gástrica.—Este arroz del *Dewa* ha sido particularmente tóxico, administrado en muy diverso tiempo de su cocción, por la vía gástrica, preparando previamente, por irritación, el aparato digestivo—en algunos casos hasta sin preparación.

Todos los curieles en los que experimentamos este arroz, por esta vía, murieron.

La irritación gástrica e intestinal ha sido provocada de diversas maneras: administrando pequeña cantidad, (una sola vez), de una solución clorhídrica débil, (3 a 5 por ciento, en agua, o en alcohol diluído; o pimienta molida en bastante cantidad.

Por lo general no se dió el arroz hasta estar seguro de que el curiel estaba bien; horas, o uno o dos días, después de administrar el irritante.

El arroz hay que ponerlo, ya preparado, en la boca del curiel, pues raras veces lo comen espontáneamente, y el líquido, rico en los principios tóxicos solubles, se da por medio de un gotero.

Administramos el arroz, una sola vez, diariamente, por lo general por la mañana, en dosis variable, lo más corriente, 15 ó 20 c. c. o más, del agua de arroz, y otro volumen igual del grano, en muy diversos días de preparación, 2, 3, 4, etc., aunque por lo general, usamos el preparado, entre los 3 y los 8 días, en que es mayor su virulencia.

Lo más importante en todas estas experiencias, es que se mantienen, constantemente, a los curieles, en la condiciones de vida acostumbrada. La alimentación habitual les fué dejada abundante. Nunca dejaron los curieles, si se ponían en sus cajas, inmediatamente después de administrado el arroz virulento, aun en dosis considerables, de comer con avidez la yerba o maloja que tanto les satisface. Sin embargo, por lo general, dejamos un período de 1, 2 ó 3 horas antes de volverlos a su dieta acostumbrada.

Los fenómenos presentados fueron los mismos que los ya descritos producidos por otras vías de inyección, pero, en todos los casos de esta vía gástrica, durante las crisis, medianas, graves, o gravísimas, se ha manifestado un síntoma muy importante, la paresia de las extremidades posteriores, paresia que nunca encontramos, intensa, entre los síntomas producidos por la vía intraperitoneal o intracraneana. La paresia se manifiesta por dificultad en sostenerse sobre las patas posteriores, cuando camina, tambaleándose el cuarto trasero durante la marcha; a veces les obliga a preferir la inmovilidad, pero, entiéndase bien nunca llega a haber parálisis.

Esta paresia, así como cierto grado de inconciencia y los trastornos respiratorios, erizamiento, etc., dura horas, hasta 10 y 12, pero al fin pasa, para reproducirse, siempre con gran aspecto de gravedad, después de unos días; son verdaderas crisis que se repiten muy graves, 2, 3, o más veces, sin que, ya lo dijimos, haya periodicidad fija en la época en que viene cada crisis, producida tras la toma del arroz virulento, no suspendido, sino ocasionalmente, en su diaria administración; al fin, en una de esas crisis, la gravedad se hace extrema, y la agonía aparente de tantas ocasiones se hace efectivamente mortal.

En la autopsia encontramos; exudado pericárdico, hasta 0.5 c. c.; y, peritoneal, hasta 4 y 5 c. c.; en cambio, en ningún caso hubo exudado pleural(?).

? Cuál es la patogenía de esos fenómenos de intoxicación por la vía gástrica, presentados por ese grupo experimental; vía gástrica, única por donde ha de infectarse el hombre, de beriberi?

Aunque creemos que seguramente esos fenómenos han de obedecer a algún mecanismo en el que juegue principal papel la preparación del elemento nervioso, no nos ha sido posible comprobar la oportunidad en que aparece esa condición.

En nuestras experiencias por vía gástrica, ante los efectivos y numerosos hechos de muerte (10 casos), provocados por el arroz, no hemos podido dilucidar, si para que exista la predisposición al tóxico—me refiero exclusivamente en la producción de forma aguda—ha de haber, solamente, irritación especial de la mucosa gastro intestinal para que el tóxico actúe sobre los filetes nerviosos, o también, alguna especial sensibilización de estos filetes nerviosos.

Unas veces—pocas—las administraciones del arroz virulento mataron a los animales, al poco tiempo—uno o dos días—de habérseles administrado el irritante de la mucosa digestiva, tal parece que por acción directa del tóxico sobre el elemento nervioso irritado. Recordemos que este mecanismo ha sido comprobado múltiples veces en la producción de diversas polineuritis. Babinski [1] al tratar sobre las neuritis periféricas, en un importantísimo capítulo, dice, que a veces hay acción electiva de las substancia, tóxicas sobre los extremos periféricos nerviosos, lo mismo que una infección, o una intoxicación, pueden obrar, localmente, sobre esos nervios; y, también Pitres y Vaillard dicen: "contrariamente a la opinión generalmente aceptada, los nervios sufrens muy fácilmente, cuando se les pone en contacto con ciertos reactivos (químicos, tóxicos), las alteraciones nutritivas y degenerativas que se tiene costumbre de considerar como efectos de la inflamación."

Pero, también es cierto, que otras veces—en la mayoría de nuestros casos experimentales por la vía gástrica—al empezar la administración del arroz tóxico, los animales no revelaron ningún síntoma, aun cuando previamente les dimos substancias irritantes gástricas, y a pesar de ingerir, diariamente, y durante muchos días—12, 14 y más—grandes cantidades del arroz virulento, hasta que, un día, tras la administración del arroz, estallaron los síntomas tóxicos, poniéndose graves, pareciendo inminente la muerte. Desde este primer ataque, que siempre pasó—ya lo hemos dicho—se repitieron otros, mientras administramos el arroz tóxico, sin periodicidad en la época de las apariciones sucesivas, hasta morir en uno de ellos.

¿Se ha producido en estos casos, en que trás la irritación preparatoria, no se presentaron fenómenos mortales con las primeras administraciones del arroz virulento, una sensibilización tardía, especial, del elemento nervioso, producida por esas primeras administraciones del arroz virulento ?

Exudaho.

Curiel.	Cavidades pleurales.		Pericardio.	Peritoneo.
	Derecha.	Izquierda.		
	C. c.	*C. c.*	*C. c.*	*C. c.*
No. 4, 1a8	0.0	0.0	0.5	1
No. 5, 1a8	.0	.0	.25	4
No. 7, 1a8	.0	.0	.1	5
No. 8, 1a8	.0	.0	.5	(?)
No. 5, 2a8	.0	.0	.2	Gotas.
No. 6, 2a8	.0	.0	.0	.0
No. 8, 2a8	.0	.0	.1	(?)
No. 9, 2a8	.0	.0	.1	Gotas.
No. 10, 2a8				
No. 11, 2a8	.0	.0	.1	Gotas.

[1] Babinski, Capitulo en el Traité de médecine de Charcot, Bouchard Brissand—Neuritis periféricas.

Por lo demás, congestión pasiva subcutánea, y muy notable de los afluentes de la vena cava superior; corazón derecho dilatado; diafragma alto; pulmones, por lo general pálidos, a veces más o menos intensamente congestionados, con zonas hemorrágicas. El corazón muy rojo y vascularizado; estómago y parte del intestino delgado contienen exudado gleroso con partículas de arroz, y muchos hematies, que pueden ser tanto de origen congestivo como debido a lesiones post-mortem; alguna congestión del intestino delgado y del mesenterio correspondiente. A veces al corte, los pulmones parecen insuflados, crepitan, y recuerdan los pulmones de la anafilaxia suérica.

El proceso total, desde la primera dosis del arroz virulento, por la vía gástrica, hasta la muerte del curiel, en estos casos prolongados, a crisis repetidas, ha durado prácticamente *dos meses;* hubo un caso de 1½ mes, y otro, prolongado, de 4 meses, sin que presentaran nunca atrofia ni parálisis, ni—salvo caso excepcional—emaciación.

Y terminamos, señores, sin pretender por un momento, que hayamos dado sobre el importante problema de la etiología del beriberi, valiosas conclusiones.

Sólo hemos querido exponer, modestamente, ante ustedes las pruebas y contrapruebas que anteceden, y que son sugestivas, porque en medio del complejo aspecto del asunto tratado, se destaca, sin embargo, determinada uniformidad.

A la inconstancia o a la poca intensidad de los casos humanos, ha correspondido el fracaso en encontrar muestras de arroz virulento en el sentido en que lo hemos venido estudiando; y, en cambio, a la intensidad y mantenimiento del brote epidémico ha correspondido la virulencia del arroz recogido. ¿Es pura coincidencia, o se tratará de una verdadera relación de causa a efecto?

A la investigación respondieron las muestras virulentas del arroz, de manera igual, precisa: presencia de un germen-fermento a esporo resistente a la temperatura de ebullición—por lo tanto, arroz no esterilizable por la cocción; producción en ese arroz cocido de substancias que matan a los animales experimentales, de manera brutal, con paresia de las extremidades posteriores, fenómenos cardio-pulmonares, lesiones agudas del corazón, derrames serosos, principalmente pericárdico.

¿Escapará el hombre a semejante proceso?

Indudablemente habrá causas que influyan en activar la producción del tóxico, o en poner la mucosa gastro-intestinal en condiciones de mayor o menor sensibilidad del elemento nervioso sobre el que parece actuar el tóxico, de manera que la acción de éste se manifieste más o menos rápidamente grave, mortal.

No debemos olvidar, para explicarnos posibles mecanismos, que también en el aparato digestivo de los grandes consumidores de arroz hay gran cantidad de este grano sobre cuyos principios amiláceos deberán actuar los fermentos que en grandes cantidades hemos visto contiene cuando está infectado, resultando de este modo el organismo preparado, para que sobrevengan formas crónicas o sub-agudas, o para que—si se producen algunas de las causas predisponentes, aun no bien determinadas, a que aludimos en el párrafo anterior—estalle la forma aguda.

Le Dantec [1] encontró gran cantidad de arroz, sin digerir, en excrementos beribéricos, y de ellos aisló un germen amilozimo. Por otra parte Metchnikoff, con sus importantes estudios sobre la flora útil intestinal, da fundamentos para pensar que es posible la aclimatación de un germen amilozimo, en un intestino cargado de material amiláceo, de la misma manera que se provoca la aclimatación del bacilo bulgárico para sus útiles actuaciones sobre la leche.

Resulten no ciertas estas consideraciones apuntadas, no del todo hipotéticas, sino fundadas en razones lógicas de analogía, y en pruebas experimentales, la intención definitiva y concluyente de este trabajo, es exponer, que en el estudio de los gérmenes amilozimos que se encuentran en el arroz, y en el analítico y exprimental de las substancias tóxicas que producen, hay que buscar más, antes de dar por cerrados los capítulos importantísimos de la patogenia y etiología del beriberi.

[1] Le Dantec: Pathologie exotique.

The CHAIRMAN. The reading of the next paper, by Mr. R. R. Williams, of the Bureau of Chemistry, on "Chemical Nature of the Vitamines," will conclude the symposium. I take great pleasure in relinquishing the chair to that distinguished investigator of Cuba, Dr. Lebredo. Dr. Lebredo will preside.

CONCERNING THE CHEMICAL NATURE OF THE VITAMINES.

By ROBERT R. WILLIAMS,
Bureau of Chemistry, Washington, D. C.

The difficulties involved in the isolation of vitamines from yeast or rice polishings have proven so serious that success seemed doubtful until a clearer idea should be gained of the chemical nature of these interesting and important substances. Accordingly attention has been directed to the preparation and testing of synthetic substances, which appeared likely to display some curative properties similar to the vitamine fraction of natural foodstuffs.

Two facts were considered of primary importance in determining the direction of the work. The first of these was that the curative substance is probably a pyridine derivative, since the curative fraction of rice polishings contains nicotinic acid,[1] and has been found to develop a pyridine-like odor.

The benzene or six-carbon atom ring is found in many tissues of all forms of plant and animal life. It constitutes an integral part of most proteins, and in plants occurs widely in the form of tannins, or the extractives which give distinctive colors, odors, and flavors. Heterocylic nuclei containing nitrogen, notably pyrrol, indol, purine, and pyrimidine, are encountered very generally in animal tissue. On the other hand the pyridine ring, consisting of one nitrogen and five carbon atoms, has a very limited distribution.

Many natural vegetable bases are pyridine derivatives, including most of the powerful alkaloids, such as nicotine, strychnine, and atropine. However, such substances are of a strictly limited occurrence, and no one, so far as I am aware, has suggested that any pyridine derivative may have any general importance in normal physiological processes.

A second hint was found in the fact that the blue color reaction given by antineuritic foodstuffs when treated with phosphotungstic acid and alkali seems to be rather closely associated with the potent constituents.[2] Since this reaction and the similar reaction with phosphomolybdic acid [3] are known to be produced by substances containing hydroxyl groups in the benzene ring, it was not surprising to find that hydroxyl derivatives of pyridine also give one or both reactions according to the number and position of the substituted hydroxyl groups.

Accordingly a series of pyridine derivatives was prepared and the therapeutic action of each individual roughly tested on polyneuritic pigeons by the administration of doses of from 1 to 10 milligrams by intramuscular injection. In some cases doses of 10 to 100 milligrams were administered by mouth as a supplementary test. The series included nicotinic, cinchomeric, quinolinic, 6 hydroxy nicotinic and citrazinic acids, α hydroxy pyridine, glutazine, 2, 4, 6, trihydroxy pyridine and its

[1] Suzuki, Shimamura, and Odake. Biochem. Zeitsch. (1912) 43, 89. Drummond and Funk, Biochem. Jour. (1914), 8, 598 and elsewhere.

[2] Funk, loc. cit. Folin and McCallum, jr. Jour. Biol. Chem. (1912) 11, 265; 13, 363.

[3] Folin and Denis. Jour. Biol. Chem. (1912) 12, 239. Funk and McCallum. Biochem. Jour. (1913) 7, 356.

anhydride and finally 2, 3, 4 trihydroxy pyridine and the so-called tetrahydroxy pyridine.

Nicotinic, cinchomeric, and quinolinic acids were prepared by the oxidation of nicotine, quinine, and quinoline, respectively,[1] and citrazinic acid from citric acid.[2] The methods of Pechmann and Stokes [3] were followed for the preparation of ethyl amino β hydroxy glutamate, glutazine, 2, 4, 6 trihydroxypyridine and its anhydride. Tetrahydroxy-pyridine and 2, 3, 4 trihydroxy pyridine were produced by the method of Ost [4] from the nitroso derivative. In the distillation of meconic acid for this purpose the modification of Peratoner and Leone [5] was used. Better methods than those of Ost are offered by Peratoner and Castellana [6] for the production of hydroxycomenic acid, from which by suitable modification of Ost's second method fair yields of 2, 3, 4 trihydroxypyridine may be obtained. These methods are being studied, as are those of Collie,[7] Tickle and Collie,[8] Lapworth and Collie,[9] and Baron, Remfry, and Thorpe.[10] Coumalic acid was used for making 6 hydroxynicotinic acid,[11] by the distillation of which α hydroxy pyridine is readily obtained.[12]

The test animals used were pigeons in which polyneuritis was developed by feeding *ad libitum* on white rice. In all cases the disease was allowed to run its course till the animals were unable to stand or make controlled movement of the legs or wings. In such cases death usually follows within 24 hours and may occur at any moment. A number of times birds died in the experimenter's hands before treatment could be administered. During and after treatment the birds were continued on a diet of white rice, and under such conditions a redevelopment of the symptoms can be only a matter of a few days. Since forced feeding was not resorted to on account of the time necessary to care for a large number of birds in this way, it was occasionally the case that the pigeons became very weak and emaciated before the symptoms developed to the desired point. Such cases are not of course strictly comparable with those of sudden development in which the animals retain a great deal of their original strength and vigor, though losing muscular control, and a measure of uncertainty is thereby introduced in occasional cases. On treating polyneuritic pigeons with the substances above mentioned definite evidence of curative power was noted in the case of α hydroxy, 2, 4, 6 trihydroxy, and 2, 3, 4 trihydroxy pyridine. The remainder of the series showed no effect. But as will be seen later such negative evidence in the case of any hydroxy pyridine derivative can not be regarded as conclusive. The first of the curative substances tested was α hydroxy pyridine. Three birds were treated with excellent results. Three others, however, showed little or no improvement. On proceeding with the series to the polyhydroxy compounds a rapid striking cure was obtained with a preparation of 2, 4, 6 trihydroxy pyridine, followed by several partial or complete failures. A second and third fresh preparation, however, produced two and three fairly rapid cures, respectively. A single fresh preparation of 2, 3, 4 trihydroxy pyridine was administered to three pigeons simultaneously, one pigeon receiving 2 milligrams, the second 1 milligram, and the third one-half milligram. The following morning the first bird was dead, while the second and third had completely recovered from all paralytic symptoms.

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[1] Weidel. Annalen (1873), 165, 330. Weidel and Schmidt Berichte (1879), 12, 1146. Hoogewerff and Dorp. Rec. Trav. Chim. Pays Bas. (1882), 1, 107.

[2] Behrmann and Hofmann. Berichte (1884), 17, 2687.

[3] Berichte (1885), 18, 2291, and (1886) 19, 2694.

[4] Jour. f. Prakt. Chem. (1879) (2) 19, 203, and (1883) (2) 27, 257.

[5] Gazz. Chim. Ital. (1894) 24, II, 75.

[6] Idem (1906) 36, I, 21.

[7] Jour. Chem. Soc. London (1891) 59, 617.

[8] Idem (1902) 81, 1004.

[9] Idem (1897) 71, 838.

[10] Idem (1904) 85, 1726.

[11] Pechmann and Welsh Berichte (1884) 17, 2384.

[12] Pechmann and Baltzer Berichte (1891) 24, 3144.

In each case all the cures obtained were of those pigeons which were first treated with a given preparation, while those treated with the same preparation a few days or weeks later invariably received no benefit. It was obvious that the substances had changed in some manner so as to lose the curative power. As there was no evidence of decomposition, it seemed probable that it was due to a tautomeric change; that is, a rearrangement of the grouping of the atoms without any actual disruption of the molecule into simpler substances. Such rearrangements are well known in many chemical substances, and have greatly interested organic chemists for the past decade. No emphasis has been laid on the possibility of a biological significance of such transformations, though they appear to be just such reactions as might easily occur within the animal organism. Many of them take place with the greatest of ease and without resort to the violent methods ordinarily employed in our laboratories.

The existence of such a tautomerism in the hydroxy pyridines has long been recognized in a general way. It has been observed that these substances under certain circumstances react as hydroxy or enol compounds, under others as ketones. However, no one has regarded it possible that the two forms could exist in a free isolated state as two distinct individuals. Each of the hydroxy pyridines is described in the literature as one substance of definite though dual properties. A critical examination of the literature, however, suggested that this was not the case. It was therefore decided to study the tautomerism of some one of the curative substances more thoroughly than had been done previously. For this purpose α hydroxy pyridine was chosen. This substance has been administered to about 80 pigeons under varying conditions and certain important facts have come to light.

It is prepared by fusing 6 hydroxy nicotinic acid and distilling the residue after the evolution of carbon dioxide has ceased. The oily distillate presently solidifies to a mass largely made up of prism crystals but often containing a few needle forms. The residue condensing in the neck of the distilling flask after completion of the process always crystallizes in the form of needles. The crystalline mass of prisms on being melted and allowed to cool, again solidifies to a mass, now consisting largely of needles. If this remelted mass is dissolved in benzene and recrystallized therefrom by the addition of ligroin, needles are found to predominate in the beautiful crystalline precipitate. With care the needles may be obtained absolutely free from prisms. From the mother liquor on concentration prisms separate and may be obtained in a pure form by filtering from the hot solvent, as the small residuum of needles dissolves freely in the hot mixture of ligroin and benzene. The needles after washing freely with petroleum ether and drying rapidly in a vacuum desiccator, melt sharply at 106° to 107°. The prisms melt at the same temperature but less sharply, and the melting point varies slightly with the speed with which the temperature of the melting point bath is raised. Evidently prisms are converted into needles very rapidly by dry heat. On allowing the solid needle form to stand for a few days in an open vessel or cork-stoppered bottle, it will be found that the crystal form has undergone a change. The needles which were originally clear and sharply defined are marked by transverse lines of cleavage. In the course of 10 to 20 days they become roughly needle shaped aggregates of prisms. The rate of this change seems to depend greatly on the amount of moisture in the atmosphere surrounding the crystals. By exclusion of moisture the transition takes place much more slowly, if at all. A water solution of needles on slow evaporation deposits only prisms.

If the two forms of crystals are titrated in the cold with alcoholic bromine according to the method of Kurt Meyer [1] neither absorbs appreciable amounts of bromine instantaneously. The prism form absorbs bromine gradually and the needle form still more slowly. Neither form can therefore be the hydroxy or enol form. However, on dissolving either form in an excess of alcoholic sodium hydroxide of known strength

[1] Annalen (1911), 380, 212.

and titrating in the cold with bromine, instantaneous absorption occurs in excess of that required by the caustic soda. α hydroxy pyridine in alcoholic sodium hydroxide solution is unquestionably largely in the enol form. Presumably all the metallic salts are likewise enols, a presumption which is in accord with the known facts in regard to other enol-keto tautomers. If the cold alcoholic solution of the sodium salt is just neutralized with cold alcoholic hydrochloric acid, detectable amounts of the free enol form are momentarily present as determined by bromine titration. The existence of any considerable proportions of the enol form in the free state appears to be brief in all neutral solvents and no method has been found for its isolation. Since α hydroxy pyridine is a base as well as an acid, it forms well-defined salts with strong acids. Whether these salts are partly salts of the enol form can not be determined by titrimetic methods since the presence of the acid makes the determination of an end point impossible. If these salts are not partly enols they are at least transformed into enols with the greatest rapidity during titration.

It therefore appears that there exist not two but three tautomeric forms of α hydroxy pyridine for which we may readily imagine structural formulæ [1] expressing intramolecular rearrangement. However, in the present state of our knowledge no useful purpose would be served by attempting to assign a definite pictorial representation to each of the three forms.

By simple means we may cause any desired form to predominate and may pass through the cycle repeatedly. Each exists in equilibrium with the others in relative quantities depending on conditions. We shall understand their relationships fully only after finding a method for determining each of the three forms quantitively under varying conditions. At present we can measure only the amount of enol.

To a degree it has been possible to determine the curative power of each of the three forms. Several preparations of freshly crystallized needles dissolved in water immediately before injection have been administered to 14 polyneuritic pigeons in doses of 1 to 2 milligrams. Improvement or cure resulted in every case, as evidenced by change in weight, paralytic symptoms, and appetite. In general, the action appears to be of the same character as that of unhydrolysed extract of rice polishings, though somewhat more rapid. Most of the birds reached an optimum from 1 to 3 days after treatment, and after a single dose of 1 to 2 milligrams lived from 5 to 10 days. Three birds were partially cured a second and third time after redevelopment of severe symptoms and lived 11, 13, and 15 days, respectively, after the first onset of the disease. However, six cures differed markedly from the others obtained with α hydroxy pyridine. The first evidences of improvement were noticed in from 40 minutes to 2 hours after injection, when the animals began to assume nearly normal attitudes. At intervals spasms of spastic movement occurred, which gradually became less frequent and less prolonged, and in the course of from 3 to 12 hours ceased altogether. After this time the birds did not differ markedly in condition from those in which less rapid cures were obtained. The gain in weight and other evidences of improvement were of the same character. The rapid cures obtained with 2, 4, 6, trihydroxy pyridine above reported were attended by the same symptoms. Protective experiments on healthy birds on a white-rice diet have not yet been made.

The physiological effect of the enol form can only be guessed so long as it remains impossible to obtain it free from the other forms and in a more or less permanent state. Injections of 1 milligram in caustic-soda solution produced fairly rapid cures in two birds so treated. Administration by mouth of 10 milligrams in caustic soda followed by dilute acetic acid also effected more rapid cures than the needle form usually gives. The silver salt was also administered to three pigeons in doses of 20 milligrams each, followed by salt solution as an antidote for the silver. Two had recovered from the paralysis the following day and lived 3 and 7 days, respectively. One died 5 hours

[1] Kaufmann Berichte (1903) 30, 1062. Decker, J. Pr. Ch. (1900) 62, 266.

after treatment. No very satisfactory conclusion can be drawn from these experiments on account of the disturbing factor of the toxicity of caustic soda and silver. The former produced severe inflammation of the tissues with which it came in contact, and the latter evidenced a general toxic action as was to be expected. Nevertheless, there was indubitable relief of the typical paralytic symptoms, and this action on the whole appeared as rapid as that obtained by treatment with the needle form. I was led to suspect that the enol form is the rapidly curative one and that the needle form is beneficial by reason of its gradual transformation into the enol in the tissues. However, this is very uncertain.

The prism form has been tested on some 30 birds under varying conditions. Doses of from 0.5 to 100 milligrams have been tried by injection and by mouth. Injections in water have been made immediately after solution, after standing several days, after boiling, and after heating under steam pressure. Injections in mineral oil and in fatty acid have also been tried. In no case was there the slightest evidence of any benefit. When large doses were administered, the action seemed distinctly adverse in several cases, as the birds died sooner than was expected. Doses of 10 milligrams injected into healthy birds, however, produced no gross toxic symptoms.

This absolute lack of curative properties is very striking and suggestive. It is apparent from the experimental evidence that the tautomeric forms exist in equilibrium and that there is fairly rapid transformation in any direction. One would therefore suppose that the prism form would, when injected into the body, rapidly convert itself into the curative form as the latter was removed from solution by absorption in the tissues or fluids requiring it. That such is not the case suggests very strongly that the pathological conditions of polyneuritis are not due to a deficiency of a substance *per se*, but to a lack of a certain type of potential energy which only that substance can supply. In other words, one is led to surmise that it is the potentiality of tautomeric change that produces the desired result. In this connection it is interesting to note that many purine and pyrimidine derivatives, some of which Funk has reported to be partially curative for polyneuritis,[1] are also theoretically capable of a similar tautomerism. That these substances are to a greater or less degree enol-keto tautomers is very strongly indicated by well-known reactions of uric acid, for example. The existence of a third tautomer is not excluded by theoretical considerations, but lacks the support of any experimental evidence.

It appeared not unlikely that other hydroxy pyridines might prove more easily controlled. Accordingly β and γ hydroxy pyridine and α α dimethyl γ hydroxy pyridine or γ lutidone have been prepared and are being tested. They show curative properties only under certain conditions. Each crystallizes in two different forms and forms metallic salts which absorb bromine rapidly in cold alcohol. In every way they appear to be strict anologues of α hydroxy pyridine

Dr. LEBREDO. The discussion is now open on these papers. I will ask Dr. Guiteras to preside.

Dr. M. X. SULLIVAN. For about six months I have been working on this question of the vitamines, and I think we have a few points that might be rather interesting to this gathering. One that stands out particularly in my memory is the fact that the mode of preparation has a great deal to do with its being effective in keeping off these polyneuritic processes. In Boston Dr. Voegtlein and I reported a paper showing that if you kept hens on corn bread made out of corn not highly milled and baking powder that the hen would run at least 165 days; but, if in addition to the corn meal a certain

[1] Jour. Physiol. (1913) 15, 489.

amount of milk was added by doubling the amount of baking soda, in 14 days it would bring about polyneuritis in the hen. That is rather striking, because we have added to the diet milk, which of itself is a protective agent; but we have doubled the bicarbonate of soda used, and this in the process of baking the bread destroys the protective kernel, so that in 14 to 20 days we were making these hens polyneuritic with corn bread, showing that the method of preparation of the food makes a difference in its effectiveness in protecting the individual. We can not say that we have the pure vitamine, because we do not know what the pure vitamine is, but we have been working on a number of things that we got out of liver, peas, and beef that was prepared by Dr. Seidell, and one of the most active that we got came from wheat bran by hydrolysis with acids, not very strong hydrolysis and not very strong heating, but it was by hydrolysis.

Dr. CLARK. A significant point was raised by Dr. Sullivan in his remarks on the acid solutions. It is perfectly possible that by making the solution alkaline, as Dr. Sullivan did in his corn bread, that the particular element was more easily destroyed than it would be in an acid solution. I am reminded of an observation that I made a year or two ago, which may have some significance on the treatment of infantile scurvy. It has commonly been recommended that the acidity of milk should be neutralized in feeding milk to infants, and there has been a good deal of misconception as to what we meant by the acidity of milk. Determining the acidity of milk by the hydrogen ion concentration, we find it is to all intents and purposes practically a vital medium. Now Holt and some other people have recommended that in cases where limewater is not available milk of magnesium should be used; but I found that in some of the more diluted milks fed to normal infants the addition of limewater in the proportions suggested brought the hydrogen ion concentration far below the point needed by a great many bacteria and to a point where the state of the milk was changed to a very large extent and would go to pieces in some of its constituents on pasteurization. Such milks are probably more alkaline than any food which is taken in the ordinary course of events by any adult.

Dr. SULLIVAN. May I say another word? It is said that there was some confusion on the question of the vitamines, because you could heat foods like orange juice and not destroy the vitamine and you could heat milk and destroy the vitamine. It is perfectly right that this should be so. When you heat milk, you lower the hydrogen ion to such an extent that it comes in the same category as corn bread.

Dr. AGRAMONTE. I wish to say that I am in perfect accord with the opinion that this disease, beriberi, as well as pellagra,

scurvy, and others, is induced directly by malnutrition or faulty nutrition. The interesting experiments reported by Dr. Lebredo in his paper, presenting an organism, an extremely resistant bacterial organism, as the producer of the beriberi toxin or the producer of an anaphylactic substance, is new to me, as, of course, to all of you who hear this for the first time, and I think should be reserved for future corroboration or confutation as the case may be. The germ theory of beriberi, I think, has been exploded a long time ago, and we need not, therefore, go over the old matter here.

We ought always to take into consideration the personal equation in dealing with these diseases of systemic disturbance and with all infectious diseases. We know that a number of individuals in the worst epidemics remain unaffected, resistant to disease, and that has been really one stumbling block in considering beriberi. For instance, we have eight or ten or fifteen individuals coming down with the same disease, but other individuals who are subjected to the same exposure do not come down with the infection, and there, I think, the personal equation should be considered. In this case I think it should be considered as much as when we consider epidemics of other disease, because if we continue to say it is due simply to the lack of this or that in the diet the question immediately arises, Why have the other men subjected to the same diet not been affected with the disease, since the human race must be considered as an entity? So, I think, we must consider that the vitality of those individuals who are susceptible to disease is below par, while that of the others is a little above par.

Dr. Tom Williams. It has been stated several times that beriberi is due to a deficiency in the diet and that all individuals living on this diet and subject to the deficiency should be affected with the disease. This is a fallacy which I do not think can be exposed too often or too urgently. There is no reason to suppose that a number of individuals will all be affected in like manner by any condition. If we give strychnine to men, there are no two who will be affected exactly alike. They all die, but there will be great difference in the rapidity of the action, etc. The same thing is true when we come to infectious processes. If we vaccinate a hundred men, 95 per cent will be "takes" and 5 per cent will have to be revaccinated. In the matter of food, we all know that what is one man's meat is another man's poison. Some people can not eat eggs, some people can not drink milk, and there is no reason why we should suppose all people are going to react in the same way to food. Some one man may consume a tremendous amount of one substance and another man a very small amount. Our retention of uric acid in the system, our individual metabolism, all differs. I think there has been enough said on that point to show that just because a person is deprived of a certain chemical element

in the food, all persons under the same conditions will not behave in the same way, any more than they will do anything else. Our practical experience indicates the same thing.

I suppose in the present day and generation everybody will admit that scurvy is due to a deficiency, and you know that if you feed a man on hardtack and bacon long enough he will get scurvy; also that if we feed 500 men, as frequently occurs in sieges, etc., all on the same ration, all do not suffer in the same degree.

With regard to Dr. Lebredo's work, I want to say that I think his experiments are absolutely accurate. I do not think there is any question about his facts, but I differ with him as to the interpretation of those facts. In the first place, if you extract rice or any other substance which has proteid materials in it—rice contains a very considerable amount of proteid—and subsequently inject those substances into the body through the skin or through the peritoneal cavity, in any other way than through the mouth, you will invariably have a certain amount of toxic phenomena. You will have them particularly if you inject simple peptones. You can thus kill an animal very rapidly. The fact that the injection was at first harmless and that only after three or four repeated injections did the harmful results obtain, the fact that the harmful effect appears with paralysis of the hind legs, respiratory embarrassment, all suggest very strongly that Dr. Lebredo was dealing with anaphylaxis produced by foreign proteid, and I have not the slightest doubt in the world that he can kill animals in that way, but I do not believe that it proves that the rice taken by mouth is toxic.

Then I wish to point out very briefly the focal nature of Mr. Williams's contribution. I think Mr. Williams is the only man who has had the conception of producing these vitamines synthetically in the laboratory. He has been working steadily at it for three years, and I think this is in its scientific nature as important as Ehrlich's synthetic preparation that will kill spirochetes. It is an absolutely new idea in medicine. We have been talking about vitamines, etc., but now we are going to get them. Of course, Mr. Williams does not claim that we will get vitamines as we find them in food, because it is not known what they are; but we are on the road, and I think the reproach which has been thrown on the term "vitamine" should be removed, and that a great many physiologists who have believed that we were discussing things that we knew not whereof we were talking will now perhaps revise their opinions somewhat.

Dr. LEBREDO. I will answer briefly all remarks that have been made to me. I said to Dr. Agramonte, I have not claimed to find anything new; the only point has been that the experiment has been very striking. I presented it to the American Public Health Association several years ago. I had in mind anaphylaxis in

these experiments and made the autopsy in one case of beriberi, wishing to see if it was not anaphylaxis, because I think in beriberi more than the etiological point is that of pathogenesis. That could be proven by taking the serum of the particular case and trying it with guinea pigs, also by using different kinds of rice and different ways of experiment. I could not find anything in that experiment, and following that I used the rice when I found that the rice was toxic and truly toxic, acting not because it was anaphylactic in the way that the anaphylaxis is with the serum anaphylaxis. I have studied many, many kinds of rice in different ways, leaving them for several days, 2, 3, 4, 5, 10, and, as I said in my paper, I put into the peritoneum 20 cc. and never killed one animal. When I found this special germ that resists the temperature for 100°, I began killing the animals right along in three or four hours by injecting into the peritoneum. In my last experiments that was the most striking thing. When I give to animals rice by the mouth I do not always kill them, but when I cause some irritation in the intestinal tract, then I can kill the animals, occasionally in two or three hours after giving it, but not at other times. But it is not anaphylaxis, as I said in my paper.

In a matter more important, that of prophylaxis, I think we are all in the same boat.

Experiments were made some time ago with chickens and guinea pigs, using rice, but I never have seen them give the heart troubles and the pulmonary troubles of the acute beriberi as I have seen in those of my experiments.

I will conclude in saying that we should take great care with the diet itself. I am in accord with that theory. It is necessary to be very careful with the diet and to have it mixed, because we may have the more chronic form, but there also should be some care taken as to the rice used. There is also the packing of the rice, which is one of the chief things to be considered in future congresses, because I think in packing lies a great danger for many, many diseases, as in plague. We need to know how to have packing done to prevent the infection of the rice, which to me is one of the things that must be looked for.

Mr. H. R. Williams. There is very little further comment that I would care to make, except that I do not want anyone to misunderstand me as saying that I consider that any one of these substances actually exists in rice or yeast or any other food substance, or that it is necessarily a substance essentially of the same character. But there is some feature of these molecules which is common to them and to the vitamines, and will be so admitted when we shall eventually find out what the vitamines are.

The CHAIRMAN. Having concluded the discussion of these papers, we will continue with the reading of the last papers of the session. I will now call upon Dr. Hess.

INFANTILE SCURVY.

By ALFRED F. HESS.

In a consideration of the "deficiency diseases" we can not omit infantile scurvy. This disorder would seem to have made its appearance in the course of modern civilization since artificial feeding has replaced mother's milk to so large an extent. It is a subject of increasing importance, which concerns the health and welfare of the infant population.

As is well known, infantile scurvy practically never develops among breast-fed babies, but is encountered among those who are fed on cow's milk, and more especially among those who receive, in addition, some of the proprietary foods which are so commonly resorted to in the preparation of the milk formulæ. There has been a difference of opinion as to whether the use of pasteurized milk alone can induce the scorbutic condition. The Commission on Milk Standards, composed of experts on this subject, in its report for 1912, stated that pasteurization does not destroy the chemical constituents of milk, which is not altered by exposure to heat under 145° F. As a favorable opportunity presented itself, and as the subject had a wide practical bearing, I determined to test the validity of this opinion. Accordingly, the infants in one ward of an infants' home, where all babies are fed upon grade A pasteurized milk, which has been heated to 145° F. for 30 minutes, were separated into two groups. As regards the one group, no change was made in the diet; they received pasteurized milk, cereal, and orange juice; in the case of the others, the only change made was to discontinue giving orange juice.

Without going into detail, the results may be summarized by the statement that almost all the infants who did not receive orange juice developed a more or less marked form of scurvy, whereas those who continued to receive the juice remained entirely free from this disorder. The opportunities for studying this question were unique, as most of the infants had been in the institution almost since birth and remained there for a period of years, so that their condition both before and subsequent to this test could be thoroughly observed. It should be added that in an investigation of a disease such as scurvy, metabolism studies are not well suited, on account of the slow course of the illness, but that clinical observations of the effect of diet or chemical analyses of the ultimate constituents of the body are far more reliable. These results were published in detail. However, in view of the fact that they were questioned by some, another test of the same character was carried out in the subsequent year. The results were the same; so that I feel safe in stating that a diet of pasteurized milk leads to the production of scurvy in infants unless some antiscorbutic food is also given. This scurvy is not as a rule the classical florid type such as is frequently met with in infants fed upon proprietary foods for months, but may be termed *latent or rudimentary*—there is a gradually increasing pallor, a failure to gain in weight, the development of some petechial hemorrhages, and, in the more marked instances, the classical superiosteal hemorrhages. It would seem probable that this insidious type of scurvy is far more common among infants than is generally recognized by physicians, and that there are many suffering from slight nutritional disturbances which may be ascribed to this cause. When the pasteurized milk was replaced by raw milk, the scorbutic condition improved, although it may be added that raw cow's milk was not comparable to orange juice as an antiscorbutic.

It is not to be inferred from these conclusions that the use of pasteurized milk is fraught with danger, but merely that it is an incomplete diet for babies and must be given with antiscorbutic food. Its use is highly desirable and to be recommended for pasteurization does not seem to affect the nutritional value of the milk and renders marked service in preventing the occurrence of various infectious diseases. There are secondary factors in the causation of scurvy. In the first place there is an individual variation which must be taken into account. This would seem to depend upon hereditary characteristics, upon the amount of antiscorbutic material which the infant brings with it when it comes into the world. Secondary food factors would also seem to play a part; in our experience those infants which received malt preparations seemed to be most predisposed to the development of scurvy, and it is quite possible that there is a relationship to carbohydrate diet, similar to that which Funk has drawn attention to in the case of beriberi. Whenever the connection of pasteurization and scurvy is brought forward, the statistics of various French writers who claim to have fed some thousands of babies on steralized milk without encountering scurvy, are cited in refutation of the harmful effects of heat. Without analyzing these results, it may be said that these infants were cared for in an ambulatory service and that their diet was therefore not under close observation and probably they were not observed for a sufficiently long period to detect the rudimentary form of scurvy which we have just outlined.

Infantile scurvy differs clinically from the other "deficiency diseases" mainly in the fact that it is characterized by the production of hemorrhage in various parts of the body, hemorrhage into the gums, into the skin, beneath the periosteum, into the kidneys, etc. A study of the pathogenesis of these hemorrhages has shown that they were not the result of alterations of the blood itself, a delayed coagulability, or a decrease of blood platelets, but that they were due to the alteration of the blood vessels which allow the blood to traverse its walls. This alteration probably should be regarded merely as a part of the general tissue changes which occur in this disorder.

Although hemorrhage is not encountered on beriberi, another typical "deficiency disease," a careful consideration will show some clinical relationships between these two diseases. As is well known, signs of involvement of the nervous system are the characteristic manifestations in beriberi. A study of the cases which came under our view showed that infantile scurvy is not entirely free from nervous signs. The knee jerks are increased, there seem to be slight involvement of the optic disks in some cases and perhaps sensitiveness of the cutaneous nerves. Again, dilation of the right heart, a remarkable pathological condition which has been frequently described in beriberi and noted by Andrews in infants who had suffered from this disease, was found to occur likewise in infantile scurvy, as demonstrated in numerous Roentgen ray examinations. Oedema, which is such a common symptom in beriberi, is not infrequently present in infantile scurvy. In fact, there is one form of this disorder, an exceptional type, where oedema is most marked. In this connection it should be remembered that degeneration of the nerves has been found by Ingier in some animals suffering from scurvy, that Holst and Froelich have noted that guinea pigs fed on decorticated or highly milled rice, developed scurvy and not beriberi, and that Darling has reported that in some African negroes a diet that caused scurvy in one set of men, caused neuritis in others. There is evidently, therefore a definite interweaving in the symptomatology of these two deficiency diseases. As is well known, beriberi is produced by a diet of decorticated rice and may be cured by feeding the rice polishings. In this regard, there seems also to be some connection between the two diseases, for we found that the giving of wheat middlings, which may be regarded as the pericarp of the wheat, in some instances resulted in a prompt amelioration of the symptoms, although it was unable to bring about a complete cure of the disorder.

The sovereign cure for scurvy is orange juice. This juice is efficient even when it has been boiled for 10 minutes. In order to test a juice of a far less degree of acidity, a

concoction of orange peel was prepared. This was found also to possess antiscorbutic qualities and to be effective even after it was boiled. This is of interest in view of the fact that Holst and Froelich showed that only antiscorbutic substances which were highly acid, were able to maintain their potency after boiling. Potato, one of the best known antiscorbutics, was found most effective in combatting the scorbutic symptoms and might well be employed for this purpose in infant feeding where orange juice can not be obtained. For this purpose the milk should be diluted with potato water instead of plain water or the usual cereal decoctions. The commercial potato flour was found to possess no antiscorbutic properties. Cod-liver oil was also found to be wanting in this particular, as not only was it unable to cure the scorbutic condition, but infants developed symptoms of scurvy in spite of receiving this oil from the very first day when orange juice was discontinued.

In connection with this study, observations of the effect of infantile scurvy upon growth was recently carried out. These observations were continued for a period of a year or more. Three periods may be distinguished in this investigation; a prescorbutic or preliminary period of about three months, during which the infants were weighed daily and measured every two weeks; a test period embracing about four months, during which the infants received the diet of pasteurized milk and cereal, which differed from the previous diet only in the fact that orange juice was no longer given; and a postscorbutic period, lasting about six months, which dated from the time when orange juice or other antiscorbutic food was once more added.

During this entire year or more the infants were weighed daily and measured every two weeks. As far as I am aware, no similar study has been carried out. Such an investigation is possible only under the conditions which obtain in an institution of this kind where the children enter at an early age and remain for long periods. Its object was to ascertain the connection between infantile scurvy and growth—growth in length as well as in weight. As is well known and has been shown by Freund, as well as by Variot, infants are particularly tenacious as regards growth in length and not readily affected by nutritional disorders, even such as reach a considerable degree of intensity. However, this must not be regarded merely as a study of growth. It must be considered rather a study of infantile scurvy and of the effect of this disorder on growth, as numerous other conditions may affect growth. That such is the case, has been shown admirably in animals in the recent investigations of Osborne and Mendel, of McCollum and others. Where growth was retarded or stimulated at will by means of diet, but which nevertheless can not be considered to have any connection with scurvy. Scurvy and growth stunting are by no means the same either in animals or in infants. It would seem that these remarks are timely in view of a recently published study by McCollum, in which he shows that the growth factor in milk is closely linked to its casein content, and prefaces his report by drawing an analogy to infantile scurvy, although none of the animals showed any signs of a scorbutic condition. That the factors which stimulate growth are not necessarily antiscorbutic, may be inferred from other experiments. For example, McCollum and Davis showed that butter fat, even after it had been heated to a high degree, was able to induce growth and Osborne and Mendel showed that this fat can be subjected even to steam and not lose its growth producing power. Notwithstanding these results there is no doubt that butter fat in pasteurized milk does not possess sufficient antiscorbutic properties to prevent the development of scurvy.

Cod-liver oil has been found to possess growth promoting qualities of a high degree of efficiency, but there is also no question that this substance, as I have stated above, is unable to prevent the development of or to cure scurvy. All of the infants under consideration obtained milk which, as a food, has been shown to contain all the constituents necessary for growth, and almost all of them obtained cereal in addition. Particular attention was given to the fact that they should obtain a sufficient quantity of food, so that the question of starvation might not enter into the experiment. To

this end, when orange juice was discontinued—that is to say, in the second period of this test—more cereal was given or the strength of the milk mixture was increased so as to obviate this complicating factor. When the scorbutic symptoms insiduously began to manifest thenselves, among them, loss of appetite, particular attention was given to the feeding, so as to induce the infants to take a sufficient quantity, and, although it is true that the total amount which they consumed was not in most cases as great as when they were entirely well, it nevertheless reached a total quite equal to that which infants frequently consume and on which they continue to grow. In almost no case did it fall below 80 calories per kilo for any considerable period of time.

First as to growth as measured by weight. It was found that, although the infants continued to gain in most cases for a few weeks following the discontinuance of the orange juice, they soon reached a stationary plane and for months were unable to rise above this level, but increased in weight promptly when the antiscorbutic food was again added to their diet. In only one instance was there no effect upon the gain in weight during this test period. There was, however, no permanent retardation of weight, the growth impulse remaining unaffected. In fact, when the orange juice was rebegun growth as manifested by gain in weight generally took place with an abnormal intensity. These infants have been found, after the observation of about half a year, to have regained the normal level of weight. In two cases, where the infants were under six months of age and had never received orange juice previously, the necessity for adding an antiscorbutic substance to the diet was manifested by a gradual lack of gain of weight at about the eighth month of life. It is very probable that many infants fail to continue to gain at this period, the third quarter of the first year of life, for the want of this essential addition to their food, and that for this reason they fail to progress until mixed feeding is begun some months later.

As has been stated during the test of the past year the infants were not only weighed but they were also measured. This group included about 20 infants, one-half of which continued to receive orange juice, whereas the others were deprived of this food. Our results in this connection may be summarized by the statement that scurvy not only has a direct effect on the weight, but also upon the growth in length, that the orange juice contains properties corrective in both regards. This fact is more striking than the failure to gain in weight, for, as has been mentioned, growth in length is a physiological impulse to which the body clings with great tenacity and which is rarely affected, even when other functions are held in abeyance. This is true likewise in animals, for example, Aron showed that in rats, which are underfed, there is a marked loss in fat and in muscle, but the skeleton continues to grow and the total ash content of the body to increase. The same holds true, as in the case of the growth in weight, when the essential substance, the orange juice, is once more given. There is an abnormally rapid increase; in other words, the stimulus has been merely temporarily held in a latent condition. It is likewise true here that boiled orange juice is effective, and the juice of the orange peel, although it seemed that the latter lost some of its potency as a result of being heated.

The time does not seem ripe for a discussion as to the nature of the peculiar dietary substance or substances, which are clearly so essential for the nutrition of the body. It is evident that it is not one or more of the various amino acids which have been shown to play such an important rôle in the production of growth. For example, lysin and tryptophan, substances which possess most marked growth producing power, must have been present in large quantities in our diet, as it has been shown to exist in considerable amounts in the proteids of the milk. Whatever their nature, it would seem that these substances are intimately associated with the continuation of health and life and until we are able to define them more definitely, we can do no better than accept the term "vitamins" suggested by Funk.

The CHAIRMAN. The next papers are those of Dr. Calixto Torres Umaña.

LA NUTRICIÓN EN LA ALTIPLANICIE DE BOGOTÁ.

Por CALIXTO TORRES UMAÑA.

Introducción.

Todo el que haya estudiado ciencias naturales sabe que hay para cada organismo una fisiología normal o patológica que le es peculiar y que esta fisiología reviste modalidades distintas que cambian con la raza, el clima, la alimentación, etc. Como consecuencia de estas modalidades fisiológicas vienen también variaciones en la higiene, en la patología, en la terapéutica, etc., cuyo conjunto constituye toda una medicina nacional o regional.

Hasta hace poco tiempo vivíamos nosotros de las investigaciones hechas en Europa y todavía hacemos muchos de nuestros estudios de medicina sobre la base de una fisiología que no nos pertenece. No pocos estudiantes aventajados han gastado nada más que en corroborar estudios hechos en el extranjero, energías que hubieran podido ser empleadas en resolver o tratar de resolver uno de tantos problemas que tenemos por delante, cuya solución sólo a nosotros pertenece.

Porque hay que pensar que lo que constituye la medicina nacional no son solamente ciertas enfermedades propias de nuestra zona, sino todo el cuadro nosológico que cambia de fisonomía desde que cambia de residencia.

El presente estudio que representa un trabajo más arduo de lo imaginable, es una modesta colaboración a uno de nuestros más trascendentales problemas.

Su iniciación tuvo origen en dos hechos de observación diaria en Bogotá: el descenso de la cifra de la urea en la orina y el descenso de la temperatura humana.

Mis primeros experimentos hechos en Bogotá, versaron sobre dos puntos: primero, temperatura humana; segundo, numeración de glóbulos rojos y medida de hemoglobina, o sea sobre el vehículo encargado de llevar el oxígeno a los tejidos para las combustiones; tercero, sobre el análisis químico de los alimentos, es decir, el examen del combustible; y cuarto, sobre productos de desasimilación azoada en las orinas.

Durante el ejercicio de mi profesión en Tunja, población situada a mayor altura que Bogotá, sobre todo como médico de algunas compañías de seguros, tuve ocasión de observar un mayor descenso de la temperatura en casi todos los individuos examinados.

Esto me sugirió la idea de emprender en aquella localidad observaciones semejantes a las de Bogotá, practicando análisis de orinas tan cuidadosos y completos como creo que no se hayan hecho antes entre nosotros.

Estudiando las causas del retardo de la nutrición en la altiplanicie, quise darle especial preferencia al asunto de la chicha, y al efecto aprovechó la buena acogida que dió a una solicitud mía el Señor Ministro de Guerra General Luján y emprendí experimentos a este respecto en seis soldados: experimentos que me dieron enseñanzas muy interesantes, como se verá en la última parte de este estudio.

Definición de la nutrición.

Toda célula viva funciona y se gasta. Para producir energía, para repararse, toma al medio ambiente materiales alimenticios, y después de haberlos elaborado en su interior, arroja los residuos de esta elaboración. Este doble proceso de asimilación y desasimilación, representa las funciones de nutrición celular y obedece a cambios químicos que se conocen con el nombre de metabolismo, el cual puede ser dividido en dos partes: el catabolismo, o reducción de los compuestos químicos más complicados a los más sencillos, y el anabolismo, o síntesis de cuerpos simples para formar más complicadas combinaciones.

Los actos nutritivos que se verifican en un organismo más complejo, como el del hombre, son idénticos, en principio, a los que se observan en los organismos unicelulares. Los elementos que se utilizan para la nutrición son tomados a los tres reinos, vegetal,

animal y mineral; ellos llevan al organismo los elementos necesarios para la constitución o para la reparación de los tejidos; las transformaciones que sufren estos alimentos en la economía ponen en libertad energía que se manifiesta en forma de labor, de trabajo mecánico y en algunos animales en la de luz o electricidad.

La misma constitución química de los alimentos nos da la explicación de su papel energético; casi todos ellos están formados de albúminas, grasas, hidratos de carbono, que son compuestos endotérmicos, es decir, formados con absorción de calor; y encierran por consiguiente energía latente; la desintegración de estos elementos en el organismo deja en libertad esta energía. De esta manera llenan las funciones de nutrición un triple objeto en el hombre normal: primero, mantener fija la composición de los tejidos vivos; segundo, mantener constante la temperatura del cuerpo, tercero, reemplazar la energía gastada por el trabajo del individuo.

En el niño, durante el período de crecimiento, y en la mujer durante el embarazo y la lactancia, tiene además por objeto ayudar al crecimiento de los tejidos. En los convalecientes, el trabajo de reproducción de material gastado es naturalmente mucho más intenso que en el estado normal.

Los materiales alimenticios siguen en el mundo un ciclo evolutivo, tendiente a una complicación progresiva. Los más simples no son otros que el oxígeno y el carbono del aire, que son fijados por la materia clorofiliana de las plantas verdes, bajo la influencia de la luz, y entran de esta manera en la composición de los tejidos vegetales. Luego los vegetales son ingeridos por los animales herbívoros y estos por los carnívoros. Es, pues, en definitiva, la energía solar almacenada por las plantas, la que transmite de un organismo a otro y representa el origen de la energía humana.

El organismo sirve para la transformación de la energía, y él no la retiene, como no la crea. En un cuerpo adulto, en equilibrio de peso, la energía llevada por los alimentos es equivalente a la gastada por el individuo; de ahí la concepción de Berthelot: "El mantenimiento de la vida no consume ninguna energía que sea propia a la vida." El principio de la conservación de la energía se aplica, pues, al animal tan exactamente como a la máquina de vapor.

Lavoisier había ya demostrado que el principal gasto de la energía humana tiene por origen las combustiones verificadas en el organismo. Berthelot, por el descubrimiento de la termoquimia, resolvió el problema demostrando que la nutrición se reduce a una transformación de la energía.

Lavoisier demostró que los animales viven y respiran oxígeno en la atmósfera y producen ácido carbónico; que se verifica en ellos una combustión análoga a la combustión de las materias orgánicas y que, como ésta, produce calor. De este descubrimiento, hecho por uno de los mayores genios que haya tenido el género humano, sacó Lavoisier su aforismo, que el ilustre Richet reputa como "el axioma fundamental de la biología." "La vida es una función química."

Pero la hipótesis primitiva de que las oxidaciones sólo se producían en el pulmón, fué destruída. Surgió entonces la idea de que el ácido carbónico y el agua nacían a favor de combustiones verificadas en la sangre misma. En 1837 Magnus descubrió que la sangre contiene oxígeno y ácido carbónico, lo que parecía demostrar la nueva teoría. Ludwig llegó a creer que las oxidaciones del hidrógeno y el carbono se efectuaban en la sangre; pero después de la publicación de los estudios de Liebig, en 1842, quedó establecido que no es hidrógeno y carbono lo que se quema en los tejidos, sino albuminoideos, hidratos de carbono y grasas.

Fué Liebig el descubridor de los métodos modernos de análisis; vinieron con él gran cantidad de conocimientos respecto a compuestos hidrocarbonados, entre los cuales se cuentan muchos productos de la economía animal. Estos conocimientos suministraban nociones importantísimas sobre la constitución de los alimentos, de la orina y de las materias fecales que no poseyó Lavoisier.

Liebig aplicó estas nuevas nociones de química a la resolución de los problemas de biología. Descubrió que los albuminoideos contienen ázoe, y en 1842 sugirió la

idea de que el ázoe podría ser proporcional a la destrucción de los albuminoideos en el organismo. Bilder y Shmidt fueron los primeros que hicieron experimentos sobre este asunto.[1]

La hipótesis de la producción del calor animal por las oxidaciones intraorgánicas debía dar lugar a rectificaciones importantes. Berthelot fué el primero que observó que el oxígeno absorbido por el animal no es proporcional al calor producido, y, por consiguiente, no puede servir de medida aun teniendo en cuenta, por una parte, el ácido carbónico producido y por otra, el agua avaluada por diferencia pues hay en el organismo otras reacciones que consisten en hidrataciones y desdoblamiento que son también fuentes de calor; de modo que el agua y el ácido carbónico no son los únicos productos de transformación de los materiales nutritivos, sino que hay muchos, como la urea y otros productos azoados, que resultan de la transformación de los albuminoideos.

Aun haciendo abstracción de las reacciones de hidratación o de desdoblamiento que intervienen en todos estos cambios, una misma cantidad de oxígeno como lo dicen Doyon y Morat,[2] "reacciona con producción de distintas cantidades de calor, según que obre sobre sustancias diferentes o cuando, dirigiéndose a una misma sustancia, da por resultado grados diferentes de oxidación."

El ácido carbónico producido puede corresponder también a cantidades diferentes de calor, por razones análogas.

En fin, el estado inicial y el estado final de la reacción que absorbe oxígeno y desprende ácido carbónico, puede no ser determinado por el conocimiento de los ingesta (que son los alimentos, haciendo figurar entre ellos el oxígeno absorbido) y de los excreta (o sean los productos de desasimilación por que en el curso del experimento puede cambiar la reacción de los tejidos, fijar ciertas substancias que provengan de los alimentos y eliminar otras que provengan de los mismos tejidos.

Ninguna de estas transformaciones se hace, de manera directa, es decir, que no son ni el carbono ni el oxígeno, ni mucho menos el ázoe los que van a producer el ácido carbónico, el agua y la urea; son principios inmediatos que vienen, sea de los tejidos o de los alimentos, los que por una serie de transformaciones, van a dar nacimiento a aquellos cuerpos. Ni se crea que estas transformaciones consisten todas en reacciones exotérmicas, sino que pasan también por reducciones o desidrataciones, que dan lugar a absorción del calor. En virtud de estas transformaciones, la glucosa pasa al estado de glicógeno, antes de convertirse en ácido carbónico. Pero el resultado final es siempre la producción del calor puesto que siempre una reacción endotérmica está compensada por varias exotérmicas.

Los testigos de la reacción son, pues, en definitiva, por una parte, los alimentos y el oxígeno (ingesta) que van a producirla y por otra, la urea, el acido úrico, el ácido carbónico y el agua (excreta) que constituyen el término final de las transformaciones químicas.

La consideración de la destrucción más o menos profunda que los organismos hacen sufrir a los materiales nutritivos, conduce a aproximar, en esta relación, la nutrición de los organismos superiores y la de los fermentos, en las cuales un enorme poder de descomposición da aspectos tan especiales. La descomposición de que acabo de hablar, que los organismos superiores hacen sufrir a la albúmina, a los hidratos de carbono y a las grasas y que terminan, como elementos principales, en agua, ácido carbónico, ácido úrico y urea, es una descomposición muy profunda cuyo rendimiento en energía es considerable. Es, por ejemplo, de 1,677 calorías para una molécula de glucosa (180 transformada en H_2O y CO_2). Considerando ahora la levadura de cerveza, vemos que este organismo vive a expensas del azúcar; pero en lugar de conducir este alimento hasta la baja escala de las transformaciones mencionadas, la levadura lo desdobla simplemente en alcohol y en ácido carbónico. Para una molécula de glucosa la cantidad de calor, es decir, de energía disponible, no es sino de setenta y

[1] Graham Lusk, The Elements of the Science of Nutrition.
[2] Doyon y Morat, Traité de physiologie.

una calorías. El rendimiento de energía es, pues, mucho menos considerable, porque el alcohol se lleva consigo cerca de nueve décimos de la energía de la glucosa.

En los organismos superiores hay relación entre el peso del cuerpo y el peso de la sustancia transformada. Estas relaciones, son, por ejemplo, para el hombre, de 500 a 600 gramos de materia orgánica para 60 a 70 kilogramos de peso vivo. Al contrario, entre el peso de la levadura y el peso de la sustancia transformada hay una desproporción enorme, lo cual se debe a que el fermento no hace sufrir a su alimento sino muy pocos grados en la escala de destrucción de la materia, y que, como dice Lambing[1] compensa la mediocridad del rendimiento de energía de esta operación, con la masa del alimento transformado.

Pero estas destrucciones no traen nada de específico que haga una diferencia de naturaleza entre estos organismos y los organismos superiores. Y aun las distinciones mencionadas desaparecerían si se considerara, no el peso del alimento transformado, sino la cantidad de energía suministrada al fermento por esta transformación.

"Lo mismo sucede," dice Lambling,"[1] en lo que concierne a la cantidad de materiales alimenticios consumidos y destruidos por el organismo; depende, no del aporte alimenticio, sino de la magnitud de las necesidades del organismo.

Pero se nota, en verdad, que inmediatamente después de la ingestión de los alimentos hay un aumento de las descomposiciones químicas, lo que parece estar en contradicción con la ley enunciada más arriba, puesto que sería la entrada del combustible la que produciría la combustión. Este evento se revela por la elevación súbita de las cantidades de oxígeno consumidas, como también por un balance total de calorías, mayor cuando se pasa del estado de ayuno al de alimentación. Así, en un experimento de Levy, un perro consumía, en el estado de reposo y en ayunas, 158 c. c. de oxígeno por minuto. Se le dió entonces una comida abundante compuesta de 500 gramos de arroz, 200 gramos de carne y 25 gramos de grasa. En las horas que siguieron, las cantidades de oxígeno fueron. respectivamente: 188, 204.8, 203.8, 212.1, 115, 210.7, 207.8, 209.3, 211.3, 206, 188.5, 176.8, "2." De la misma manera Voit ha notado en el hombre un gasto de calorías de 2,470 y de 2,320 (término medio 2,390) en 24 horas al estado de ayuno; mientras que con la ingestión de alimentos variados, el gasto oscilaba entre 2,350 y 2,940 (término medio 2,556), o sea un aumento de 7 por ciento, poco más o menos.

Observaciones hechas posteriormente en el ayunador Cetti, en Berlín, confirman plenamente los resultados. "Pero este aumento," dice Lambling[2] "depende únicamente del trabajo secretor y sobre todo, mecánico, impuesto al tubo digestivo, y no del aumento de las combustiones llevado por la alimentación." Sin embargo, según la autoridad no menos respetable de Lable [3] esto no parece exacto, pues el trabajo del tubo digestivo no exige sino un gasto muy pequeño de calorías, y por otra parte, la concordancia bien notada por Rübner y Atwater, entre el valor calorígeno de la ración alimenticia y la excreción calórica establece el hecho con precisión:

Mientras más coma un sujeto, más calorías virtuales ingiere, y más calorías reales gasta. Se necesitarían nuevos experimentos, instituídos en este sentido, para establecer que el gasto de calorías varía a voluntad con la ración alimenticia. De la misma manera que, en general, se ingiere una ración alimenticia excesiva, se excreta probablemente una suma de calorías demasiado grande. El equilibrio calórico podría obtenerse con una ración alimenticia más débil, aportando nuevas calorías. Lo que habría que determinar es precisamente el límite de la ingestión alimenticia susceptible de mantener la temperatura constante sin que el peso del sujeto baje y sin que esté obligado a quemar sus propios tejidos.

Se sabe que la cantidad de oxígeno consumida por el organismo es, en muy anchos límites, independiente de la cantidad de oxígeno ofrecida a los tejidos por la respiración, y que la cantidad de oxígeno gastada varía con la calidad de alimentos que se van a transformar; 100 gramos de oxígeno transforman 38 gramos de grasa en H_2O y

[1] Lambing, Traité de Pathologie Générale de Bouchard.
[2] Lambling, obra citada.
[3] M. Lablé, Les régimes alimentaires, p. 30, 1910.

CO_2, con producción de 325 calorías u 84.4 de hidratos de carbono, en H_2O y CO_2, con producción de 362 calorías. La cantidad de oxígeno pues, ni descubre la cantidad de combustible destruído ni la energía puesta en libertad. Cuando hay cierto mínimum de aporte de materiales azoados, basta suministrar un exceso de alimentos terciarios para que la necesidad de energía sea cubierta; este exceso puede ser proporcionado por las cantidades más variables de grasa o de hidratos de carbono.

Este es el cuadro esquemático de nuestras necesidades alimenticias, tal como se realiza en el cuadro esquemático de nuestros experimentos de laboratorio. Pero en la vida ordinaria, ¿cómo pasan las cosas y cómo satisfacen los hombres sus necesidades alimenticias, únicamente guiados por su instinto? Es aquí donde la noción de los alimentos isodinámicos de Rübner esclarece en gran manera la fisiología de la nutrición. Antes de la adquisición de tal noción hubiera sido imposible abordar este problema.

Sean, por ejemplo, dos individuos de los cuales el uno vive con 120 gramos de albúmina y 269.7 de grasa, y el otro con la misma cantidad de albúmina, más 611.7 gramos de hidrocarbonados. Al no comparar sino los pesos se vería que la cantidad de albúmina representada en el primer caso es de 30 por ciento, y en el segundo es 16 por ciento de la ración. ¿Cómo podría pensarse, en presencia de estos casos, que la albúmina represente en ambos el mismo papel y tenga la misma importancia?

Introdúzcase, entonces, la consideración de los valores calorimétricos, y se tendrá:

Primer caso: Albúmina, 120 por 4.1—492 calorías; grasa, 269.7 por 9.3—2,508 calorías; total, 3,000 calorías.

Segundo caso: Albúmina, 120 por 4.1—492 calorías; hidrocarbonado, 611.7 por 4.1—2,508 calorías; total, 3,000 calorías.

La albúmina ha aportado en él un caso y en el otro la misma cantidad, o sea 16.4 por ciento, de la cantidad total de energía gastada; el resto, o sea 83.6 por ciento, es suministrada por cantidades isodinámicas de grasa o de hidrocarbonados.

Rübner ha calculado de esta manera el aporte de energía de cada especie de alimentos observando en individuos que pertenecen a categorías sociales menos y menos elevadas y que suministran un trabajo más y más penoso.

El cuadro siguiente resume los resultados obtenidos: por 100 calorías suministradas por el organismo se encuentran:

	En albúmina.	En grasa.	En hidratos de carbono.
Inanición	12.1	87.9	11.0
Clases acomodadas	19.2	29.8	51.0
Carpinteros, soldados, etc	16.7	16.3	66.9
Obreros que suministran un trabajo considerable	18.8	17.9	63.3
Mineros, obreros de fábrica	13.4	21.2	65.5
Leñadores	8.3	38.7	52.8

En lo que concierne a las materias albuminoideas, se ve que la proporción relativa de calorías suministradas por ella va disminuyendo a medida que se desciende en el cuadro y esto depende de que en las clases acomodadas se hace uso de preferencia de la alimentación animal, es decir, que se consumen pesos absolutos de albúmina mucho mayor que en las menos afortunadas. Como por otra parte las clases ricas, en razón del menor trabajo mécanico, gastan menos calorías que las necesarias para un obrero, la proporción relativa de calorías tomadas a la albúmina se encuentra por esta razón aumentada en los ricos y disminuída en los pobres y en los obreros.

Para las grasas se pueden hacer consideraciones análogas. Midiendo el número relativo suministrado por ellas se ve que va disminuyendo a medida que se desciende en la escala; pero de la clase V en adelante principia a aumentar y puede de nuevo llegar hasta igualar a las clases acomodadas. Esta diminución se explica porque el obrero toma a los hidrocarbonados (almidón del pan fécula de la papa) cantidades crecientes a medida que el trabajo mecánico lo va exigiendo; pero luego, dice Rübner, llega un momento en que el volumen de los alimentos impondría un trabajo muy

considerable al tubo digestivo, el cual queda impotente para dominar una gran masa, e interviene entonces como complemento indispensable el alimento grasa, que tiene la misma ventaja y asegura un valor calorífico considerable. Agréguese a esto que las grasas son ingeridas casi en naturaleza y que representarían, por lo tanto, en una masa igual un aporte de energía más considerable que los otros alimentos. De esta manera el organismo encuentra:

En 100 gramos de carne flaca a 21 por ciento de albúmina, 86 calorías; en 100 gramos de pan a 8 por ciento de albúmina, 86 calorías, y en 5 por ciento de almidón, 258 calorías; en 100 gramos de mantequilla de 85 por ciento de grasa pura, 790 calorías.

Vienen, en fin, los hidrocarbonados admirablemente representados por los vegetales, de los cuales, por ser más baratos, toma el obrero el total de su ración alimenticia; pero por razones ya dichas disminuye el tamaño relativo de hidrocarbonados hasta 22.8 para la última categoría.

El calor de combustión de los alimentos, o sea el total de calorías suministradas por la unidad de peso, mostrado por el calorímetro no es siempre igual al que se produce en el organismo. Si se trata de grasas o de hidrocarbonados, tenemos para un gramo de sustancia, tanto en el calorímetro como en la combustión orgánica: Grasa 9.3 a 9.4 calorías; hidrocarbonados, 4.1 a 4.2 calorías, pero con los albuminoideos no sucede lo mismo, porque el ázoe, que queda en libertad en el calorímetro al estado elemental, se transforma en el organismo y se elimina bajo la forma de productos complejos, de los cuales las nueve décimas partes, poco más o menos, son urea y el resto deja el organismo bajo forma de productos menos simplificados. Hay pues que restar el calor de combustión de estos productos del de las materias albuminoideas para lo cual la mayor parte de los autores, tienen en cuenta la urea y hacen abstracción de los otros productos azoados. Como 100 gramos de materia albuminoidea, a 16 por ciento de ázoe, suministran aproximadamente 34 gramos de urea, o sea casi la tercera parte de su peso, hay que restar del resultado medio del calor de combustión de la albúmina (5 a 6 calorías) la tercera parte, poco más o menos del calor de combustión de la urea, o sea, 0.850, corrección que da del 15 al 16 por ciento del calor de combustión total. Hay que anotar, además, que el ázoe se eleva en algunos albuminoideos de 16 a 19 por ciento, lo que aumentaría la cifra de 0.85 a 1 caloría. Hechas estas anotaciones y despreciando una décima parte del ázoe que no se transforma en urea sino en otros compuestos, se puede tomar como cifra media del calor de combustión de los albuminoideos, la de 4.7 a 4.8 calorías por gramo.

Cuando se quiere valorizar el poder calorimétrico de un alimento pon la comparación de la albúmina ingerida y el ázoe excrementicial hay que hacer dos correcciones que corresponden: la una al alimento y la otra a la excreción azoada. La primera es debida, por una parte, al aumento, de algunas albúminas hasta 19 por ciento de ázoe y que el dosado de la albúmina se hace por el dosado del ázoe, y en los vegetales hay sustancias azoadas que no son albuminoideas. Por este motivo se baja el valor calorímétrico de la albúmina a 4.1 en vez de 4.8 cuando se trata de alimentos mixtos. La segunda causa de error se efectúa cuando no se hace el análisis del ázoe eliminado por las deposiciones. Rübner estima este residuo en 8.11 por ciento del valor calorimétrico total de la reacción; algunos llegan hasta el 10 por ciento para el régimen mixto. Es natural que con la alimentación vegetal, que da una mayor cantidad de residuos no absorbidos, esta cifra debe aumentar.

Con sólo dosar el ázoe total de la orina, puede medirse la cantidad de albúmina de la cual ha dispuesto el organismo, es necesario entonces tomar la cifra 4.8 en vez de 4.1 como valor calorimétrico.

Sea, por ejemplo, un individuo que elimine 14 gramos de ázoe, total en las 24 horas. Sabiendo que a 100 gramos de albúmina corresponden 16 de ázoe, tendremos la siguiente relación:

16:100::14:X, de donde $X=\frac{1400}{16}$ o a 14 por 6.25=87.50 (6.25 es el coeficiente que resulta de dividir a 100 por 16) y 87.50 por 4.8=420 calorías.

Cuando sólo se desea la urea se hace el cálculo aproximado de esta manera: peso de la urea multiplicado por 1.30 o 1.14, que es el peso del ázoe expresado en urea, y el producto multiplicado por 2.91 gramo de urea corresponde a 2.1 de albúmina).

Se obtiene de esta manera según Lambling,[1] con aproximación suficiente, la cantidad de albúmina desasimilada. Una mayor precisión se obtendrá naturalmente con el primer procedimiento.[1]

Al lado de esta teoría isodinámica o teoría de Rübner viene a oponerse la teoría de Chauveau más científica en mi concepto; y si he desarrollado más extensamente la primera es porque sobre ella están todavía reposando muchos principios de fisiología moderna y porque hasta cierto punto ésta viene a ser necesaria para el fundamento y desarrollo de la segunda.

La teoría de Chauveau que llamaré también teoría glicogénica, dice que el poder nutritivo de los alimentos se confunde con su poder termógeno o dinamógeno. La grasa no puede ser utilizada como elemento energético, sino después de su transformación en glicógeno; hay pues en este alimento una pérdida de energía sobre la que sufre según la teoría de Rübner. El glicógeno sería el estado a que tienen que llegar las sustancias alimenticias para producir energía. Es decir que un alimento es tanto más productor de energía cuanto mayor sea su capacidad para transformarse en glicógeno.

"El cuerpo que en el organismo llena la función energética," dice Morat, " es el carbono; la forma química alrededor de la cual evoluciona en esta función, es el azúcar y el cuerpo que en su conflicto con él manifiesta esta función el oxígeno. La evolución energética se encuentra como condensada en estos tres términos correspondientes a funciones que son: la alimentación, la glicogenesis y la termogenesis."

Chauveau ha demostrado y confirmado por la experimentación la teoría, demostrando que un gramo de grasa y 1.52 gramos de azúcar de caña son capaces de suministrar, la primera por oxidación, la segunda por hidratación, la misma cantidad de glicosa y por consiguiente de glicógeno; las cifras dadas por la experimentación, son exactamente las que da la ecuación hipotética de la transformación de la grasa.

Lo que se ha dicho de la grasa se aplica a todas las otras sustancias alimenticias, inclusive los albuminoideos; de aquí que haya dado a esta teoría el nombre de teoría glicogénica.

Pero según esta última teoría la grasa y el azúcar concurren a la nutrición en el mismo grado no en cuanto se les administra en cantidades térmicamente equivalentes (Rübner), sino en cantidades propias para producir la misma cantidad de glicógeno (Chauveau). En resumen, la segunda teoría le quita a la primera, el error proveniente del gasto de energía, de la pérdida de valor energético que una sustancia alimenticia necesita para trasformarse en glicógeno.

Es una conexión semejante aunque hecha en opuesto extremo, a la que se hace, según Rübner a los albuminoideos cuando se compara su valor energético real con su valor de combustión dado en el calorímetro. Proviene esta conexión, de que en el organismo no llegan los albuminoideos al mismo extremo de descomposición a que llegan en el calorímetro, sino que se transforman en otros productos de composición tan complicada como la urea.

Por no caber en el plan de mi estudio, no me he detenido a hablar de las transformaciones de los albuminoideos en el tubo digestivo. En un capítulo posterior hablaré de las distintas formas de eliminación azoadas y de la proporción en que se verifican en Bogotá y en otras poblaciones de la altiplanicie.

INFLUENCIA DEL CLIMA DE LA ALTIPLANICIE SOBRE LAS COMBUSTIONES HUMANAS.

Voy a hacer algunas consideraciones sobre los climas de Bogotá y Tunja, poblaciones donde he practicado mis investigaciones.

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[1] La ración media de mantenimiento en los hombres se divide, según la mayor parte de los fisiólogos, de la manera siguiente: Albúmina, 135 por 4.1 equivale a 553; grasa, 140 por 9.3 equivale a 1,302; hidratos de carbono, 249 por 4.1 equivale a 1,021; total, 2,876 calorías. Restando de éstas un 8 por ciento que se pierden en las deposiciones, quedan 2,646 calorías netas, o sean 36 por kilógramo.

Tomo las de Bogotá de un trabajo presentado por el Dr. Julio Garavito a las sesiones científicas de 1910 y las de Tunja, de mis observaciones personales y de datos tomados en los gabinetes y laboratorios del seminario conciliar de esta ciudad.

Haré luego algunas consideraciones sobre la influencia del clima en las combustiones humanas para lo cual servirá de mucho la comparación entre dos poblaciones de altura un poco diferente.

Bogotá está situada cerca del ecuador entre las líneas isotermas 25 y 28 grados, pero su clima puede clasificarse entre los medios o los fríos.

El mínimum de temperatura se observa a las 5 y 45 a. m. y es de 8.74 grados, y el máximum a las 2 p. m. es de 16.95. Las mayores variaciones se encuentran durante el mes de enero. La temperatura media es de 12.97 grados, la amplitud media de las oscilaciones diurnas es de 7.11.

El estado higrométrico es de 79.5 por ciento. La velocidad máxima del viento corresponde al máximum de temperatura. En los meses de junio, julio y agosto se observan golpes de viento, de corta duración, que alcanzan hasta 15 metros por segundo.

En general, se considera la presión atmosférica en Bogotá como de 560 mils. de mecurio. Según los cálculos de Garavito hay un máximun de 0.5609 y un mínimum de 0.5579. La mayor altura del barómetro se observa en los meses de junio, julio y agosto y la menor en octubre, noviembre y diciembre.

Oxígeno.—Si se considera la proporción de oxígeno en volumen, es casi igual en Bogotá y a nivel del mar (21 por ciento), pero si se tiene en cuenta, no el volumen sino el peso, es natural que la cantidad disminuya en inversa proporción con la presión. Teniendo en cuenta que un litro de aire, a la presión de 0.76, contiene 0.259 gramo de oxígeno, se obtiene poco más o menos 0.192 gramo de oxígeno por litro de aire en Bogotá.

Tunja tiene una situación y un clima muy semejantes a los de Bogotá, sólo que el estado higrométrico es más bajo en aquella y la velocidad del viento mayor.

La temperatura media es de 11.99 grados. La mayor amplitud de las oscilaciones diurnas es de 6 grados. El máximum de temperatura se observa en el mes de enero y el mínimum en julio.

La altura sobre el nivel del mar es de 2,790 metros y la presión media del barómetro de 0.536 mils. de mercurio.

Temperatura humana en la altiplanicie.—Todos los autores europeos que he consultado están de acuerdo en fijar para el hombre una temperatura axilar media de 37 grados a 37.2 grados. En Bogotá, según lo habrán observado todos los médicos y estudiantes, la temperatura media rara vez pasa de 36.5 grados; de tal manera que muchos consideran como febricitantes a los individuos cuya temperatura llega a 36.8 grados.

El Dr. Pabon en 135 observaciones que reunió para su tesis de doctorado, obtuvo un promedio de 36.5 grados, es decir, de 0.5 grado, inferior a la cifra considerada como normal en Europa. El Dr. Corpas en su tesis agrega 100 observaciones más que dan un resultado de 36.3 grados, lo que da una diferencia de 0.9 grado con la cifra de Beclard 37.2 grados.

En 86 observaciones tomadas por mí en Tunja en adultos de 20 a 40 años, pertenecientes a distintas clases sociales, obtuve un promedio de 36.24 centígrados de temperatura, con 76 pulsaciones y 20 respiraciones por minuto.

Parece pues demostrado que hay una baja considerable de la temperatura del hombre en la altiplanicie, en relación con la temperatura aceptada como media en Europa.

Todas las hipótesis que pueden hacerse para explicar este fenómeno pueden reducirse, en mi concepto, a tres: (1) Influencia de la temperatura ambiente; (2) influencia de la altura; y (3) influencia de la alimentación. Me limitaré, por el momento, a las dos primeras, para ocuparme luego de la tercera, en capítulos posteriores.

Influencia de la temperatura ambiente.—Ya dije que, según los cálculos del Dr. Garavito, la temperatura media de Bogotá es de 12.97. El Dr. Corpas cree que esta baja temperatura exterior es una de las causas de la baja de temperatura animal, pues "el cuerpo humano en busca de equilibrio térmico tiende a acercarse a ella."

A primera vista esta causa no carece de importancia, pues aunque todos sabemos que los animales omeotermos tienen medios de defensa que permiten luchar contra la temperatura ambiente, también es verdad que un descenso o un aumento considerable de temperatura pueden hacer variar la temperatura animal en algunos décimos de grado. Esto parece confirmado por los experimentos de David y los posteriores de Mantegazza, Fousset, etc.; pero ninguno de estos observadores ha hallado una baja tan considerable como la que se encuentra entre nosotros, ni aun en atmósferas de proporción higrométrica más considerable.

Entre 247 observaciones de Mantegazza, por ejemplo, no ha encontrado, en climas mucho mas fríos que el de Bogotá, sino una temperatura mínima de 36° 4′, que alcanza, cuando más,[1] a ser igual a nuestra temperatura media.

Agrégase a esto que las razas tropicales, por vivir en un clima siempre igual, luchan por efecto de la costumbre mucho mejor contra los grandes fríos como contra los grandes calores; así las pequeñas variaciones de temperatura animal que se observan en Europa del verano al invierno no se encuentran en los trópicos, al comparar a este respecto, los habitantes de los climas más ardientes con los de los más fríos; de modo que la temperatura ambiente (que no es tan baja para producir un descenso de temperatura animal), no nos explica la baja considerable de la temperatura animal en la altiplanicie.

Presión atmosférica.—Para mantener sus combustiones orgánicas, el hombre necesita introducir en cada hora según los cálculos de Brüner y Valentin 3130 gramos de oxígeno, que corresponden a 2191 litros al nivel del mar, o sea 450 litros de aire, que se introducen en las 15 o 16 respiraciones por minuto, que se consideran en Europa como normales, a razon de 500 c. c. en cada una, quitando los 50 c. c. que son expulsados a cada expiración.

Ahora bien: como en Bogotá la presión es de 0.20 cms. de mercurio menos que a nivel del mar, si el organismo no dispusiera de medios de defensa, se tendría que en los 21.91 litros de oxígeno no introduciría los 31.30 gramos, sino mucho menos; de donde resultaría una gran insuficiencia de las combustiones, que podría explicarnos la baja de la temperatura humana.

Pero hemos visto ya que la actividad del metabolismo celular es independiente de la cantidad de oxígeno ofrecido a los tejidos. Los experimentos de Liebig demuestran que la presión no influye sobre la absorción de oxigeno,[2] y aun cuando Truntz observó un aumento, este aumento no duraba sino cuando más un minuto, y era, según el mismo autor, debido a la repleción de los pulmones.[3]

De la misma manera que el organismo no toma sino el oxígeno que necesita, cuando la atmósfera está enrarecida se vale de ciertos medios de defensa para tomar todo el que le sea necesario. Veamos si de estos medios disponen los habitantes de la altiplanicie.

Bajo la influencia del clima de las alturas, "que llevaría en realidad la disminución del oxígeno del aire en relación con la presión atmosférica, el número de los glóbulos rojos aumentaría, en una gran proporción, hasta el punto de alcanzar siete y ocho millones por milímetro cúbico en el hombre." Según la observación hecha por T. Viault, en sí mismo a 4,392 metros de altura en un viaje al Perú, la hiperglobulia se produciría a partir de los 700 metros. Por medio de esta hiperglobulia aumenta la superficie de absorción del oxígeno y puede el organismo fijarlo en la misma cantidad que a la presión ordinaria. Es éste, pues, un mecanismo regulador o de defensa que se pone en juego a medida que la presión disminuye. Cuando los sujetos sometidos a los experimentos vuelven a la llanura, el número de los glóbulos rojos vuelve rápida-

[1] Ch. Richet, La chaleur animale. [2] Lusk, Science of nutrition. [3] Journal of Physiology, 1907.

mente a su nivel normal. Algunos de los hechos que han servido para la edificación de esta teoría han sido vivamente controvertidos. La cuestión, en todo caso, está todavía oscura, pero lo que parece demostrado es que la hiperglobulia de que se trata es simplemente periférica y que el número de glóbulos rojos del corazón y de los gruesos vasos no aumenta." [1]

Los siguientes exámenes de sangre, practicados, unos por mí, y otros, en su mayor parte, por el Dr. Jorge Martínez Santamaría, podrán darnos alguna idea de lo que a este respecto pasa en la altiplanicie.

Las numeraciones de glóbulos fueron hechas en el numerador de Hayem. Algunas han sido rectificadas en el Thomas Zeiss. La hemoglobina fué medida en el aparato de Fleischl.

Números.	Edad.	Glóbulos rojos por mil. cub.	Hemoglobina.	Números.	Edad.	Glóbulos rojos por mil. cub.	Hemoglobina.
			Por ciento.				*Por ciento.*
1	24	5,084,000	80	58	20	4,619,000	96
2	30	4,900,000	80	59	32	4,681,000	91
3	20	5,673,000	80	60	22	5,270,000	95
4	24	5,697,000	74	61	24	4,650,000	100
5	25	5,952,000	86	62	25	4,960,000	98
6	23	4,836,000	80	63	38	3,998,000	90
7	28	5,759,000	88	64	25	4,680,000	95
8	25	5,611,000	90	65	30	3,875,000	80
9	27	5,549,000	73	66	28	3,906,000	90
10	22	5,890,000	90	67	24	4,123,000	96
11	22	5,840,000	80	68	24	4,960,000	90
12	23	5,759,000	90	69	30	5,246,000	85
13	35	5,673,000	73	70	20	4,650,000	93
14	26	5,518,000	98	71	32	4,340,000	88
15	25	5,053,000	90	72	22	4,185,000	75
16	26	5,456,000	80	73	27	5,022,000	80
17	38	4,960,000	70	74	25	4,405,000	90
18	32	5,890,000	80	75	28	4,898,000	88
19	33	5,208,000	90	76	40	4,371,000	92
20	22	5,904,000	80	77	25	4,154,000	93
21	24	5,363,000	85	78	25	4,030,000	88
22	22	5,177,000	90	79	22	4,041,000	82
23	23	5,115,000	90	80	25	3,410,000	78
24	23	5,122,000	74	81	38	4,464,000	82
25	26	4,705,000	84	82	28	4,712,000	93
26	31	4,774,000	90	83	32	4,340,000	68
27	27	5,270,000	84	84	30	4,154,000	78
28	30	5,208,000	80	85	38	3,906,000	75
29	35	5,332,000	90	86	40	4,340,000	83
30	25	5,425,000	68	87	30	4,867,000	82
31	25	5,425,000	80	88	38	5,580,000	100
32	26	4,898,000	80	89	20	4,402,000	83
33	28	5,921,000	85	90	23	5,184,000	80
34	24	5,084,000	85	91	38	4,800,000	87
35	26	4,774,000	74	92	30	4,351,000	85
36	30	5,239,000	80	93	40	4,464,000	85
37	30	5,153,000	80	94	21	4,493,000	90
38	30	4,464,000	78	95	36	5,084,000	82
39	23	5,594,000	80	96	20	4,898,000	92
40	26	4,743,000	68	97	30	4,495,000	70
41	25	4,619,000	80	98	20	4,929,000	90
42	22	4,530,000	80	99	28	4,743,000	90
43	25	4,681,000	70	100	23	5,084,000	93
44	24	5,100,000	70	101	20	4,712,000	93
45	31	5,053,000	76	102	22	4,061,000	95
46	26	4,898,000	78	103	20	4,650,000	80
47	23	5,710,000	74	104	20	4,712,000	79
48	27	4,650,000	76	105	28	4,464,000	79
49	26	4,734,000	90	106	35	3,658,000	80
50	23	4,898,000	79	107	36	5,301,000	91
51	24	4,805,000	74	108	35	3,720,000	60
52	23	4,960,000	81	109	40	4,123,000	85
53	24	4,681,000	80	110	34	5,890,000	95
54	40	4,843,000	82	111	37	4,420,000	70
55	36	5,852,000	100	112	25	4,805,000	74
56	30	4,898,000	78	113	23	4,805,000	92
57	40	4,752,000	80	114	30	4,588,000	92

[1] Gley, Traité élémentaire de physiologie, 1910.

Números.	Edad.	Glóbulos rojos por mil. cub.	Hemoglobina.	Números.	Edad.	Glóbulos rojos por mil. cub.	Hemoglobina.
			Por ciento.				*Por ciento.*
115	25	5,401,000	93	159	37	4,153,000	76
116	23	4,805,000	92	160	21	4,929,000	78
117	25	5,573,000	105	161	40	4,371,000	74
118	23	4,843,000	98	162	25	4,774,000	81
119	23	4,743,000	97	163	20	5,246,000	79
120	20	4,743,000	65	164	30	4,254,000	60
121	20	4,805,000	70	165	35	3,813,000	74
122	21	5,238,000	72	166	20	4,154,000	80
123	40	4,681,000	85	167	40	5,084,000	92
124	36	4,030,000	92	168	20	4,519,000	88
125	24	4,280,000	90	169	40	4,588,000	75
126	30	4,563,000	78	170	37	4,550,000	92
127	21	4,928,000	83	171	40	4,650,000	85
128	20	5,549,000	90	172	20	4,340,000	61
129	20	5,580,000	79	173	35	4,061,000	81
130	27	4,433,000	74	174	20	4,495,000	82
131	33	4,436,000	69	175	22	4,537,000	98
132	32	4,495,000	86	176	22	4,011,000	76
133	26	4,836,000	94	177	25	4,240,000	70
134	35	4,247,000	76	178	35	4,488,000	75
135	23	4,929,000	85	179	40	3,999,000	78
136	20	3,503,000	76	180	26	3,937,000	84
137	40	4,712,000	86	181	40	4,241,000	74
138	40	4,619,000	90	182	23	4,185,000	68
139	28	4,836,000	90	183	20	4,003,000	70
140	25	4,701,000	85	184	28	5,095,000	70
141	26	4,512,000	80	185	25	4,937,000	72
142	20	3,937,000	78	186	20	4,375,000	80
143	21	4,327,000	81	187	38	4,537,000	92
144	28	4,495,000	76	188	33	4,589,000	76
145	40	5,146,000	89	189	22	4,490,000	80
146	23	4,533,000	92	190	22	4,750,000	88
147	40	5,158,000	80	191	29	4,240,000	76
148	20	4,712,000	92	192	30	4,125,000	72
149	20	4,309,000	93	193	32	4,495,000	82
150	25	5,128,000	103	194	47	4,488,000	82
151	22	3,534,000	94	195	20	5,086,000	70
152	23	4,123,000	62	196	21	4,650,000	85
153	36	4,371,000	82	197	22	3,998,000	76
154	40	3,906,000	70	198	40	4,589,000	75
155	24	4,998,000	104	199	20	5,246,000	79
156	40	4,307,000	80	200	25	4,929,000	78
157	36	4,829,000	89				
158	20	4,619,000	80	Promedios		4,799,714	83.21%

Hé aquí mis observaciones hechas en Tunja en individuos de 20 a 40 años.

Números.	Edad.	Glóbulos rojos (por mil. cub.).	Hemoglobina (por ciento).	Números.	Edad.	Glóbulos rojos (por mil. cub.).	Hemoglobina (por ciento).
1	29	4,100,000	82	12	39	4,650,000	74
2	23	4,800,000	80	13	20	4,759,000	80
3	31	5,053,000	72	14	38	4,219,000	76
4	35	5,139,000	78	15	40	4,130,000	88
5	40	4,560,000	90	16	22	4,650,000	82
6	30	4,389,000	68	17	30	4,420,000	74
7	26	5,530,000	90	18	32	4,340,000	88
8	28	4,357,000	73	19	18	4,405,000	72
9	29	5,100,000	72	20	25	4,030,000	80
10	33	4,498,000	74	21	22	4,284,000	72
11	38	4,120,000	74				

Promedios, 4,517,380.

Como se ve, estos 21 análisis dan un promedio de 4,547,380 de glóbulos rojos y 78 por ciento de hemoglobina, lo que corresponde a un valor globular de 26 diezbillonésimos de milígramo.[1] Para los de Bogotá y 17 para los de Tunja.

[1] El valor globular, es decir, la cantidad de hemoglobina que contiene cada glóbulo rojo, ha sido obtenido, teniendo en cuenta la densidad de la sangre, por la siguiente fórmula: $X = \frac{H \times D}{N \times 100{,}000{,}000}$ en la que X representa el valor globular; D la densidad de la sangre prescindiendo de la coma decimal (1061); H la cantidad de hemoglobina contenida en 100 gramos de sangre, y N el número de glóbulos rojos por 1 mm. C.

Desde que el Dr. Jorge Vargas Suárez practicó sus análisis de sangre, todo el mundo creyó (inclusive el autor de este trabajo) que se trataba de algún defecto de técnica, pues nadie podía figurarse que a la altura de Bogotá, hubiera una disminución de las hematías en contra de lo que generalmente se admite.

Fué pues, el Dr. Vargas Suárez quien primero llamó la atención sobre tan importante asunto y a mí me cabe el honor de venir hoy a confirmar su observación. Para mayor abundamiento, mis promedios de Bogotá y los del Dr. Vargas Suárez, dan una cifra casi idéntica, siendo de advertir que el autor de este trabajo, no tuvo conocimiento de la tesis del Dr. Vargas, sino mucho tiempo después de terminadas sus numeraciones de Bogotá.

Si el número de mis observaciones tomadas en Tunja no fuera tan inferior al de Bogotá, aquellos contribuirían a afirmar una tesis absolutamente opuesta a la sostenida por Viault y otros fisiólogos europeos; es decir, que en vez de aumentar nuestras hematías a medida que ascendemos, disminuyen.

Concuerdan estos resultados con la baja de temperatura, lo que quiere decir que nuestra raza es impotente para defenderse contra el enrarecimiento del aire en las alturas.

Pero fuera de la hiperglobulia y de la hiperhemoglobinuria hay otros medios para esta defensa que voy a analizar.

Vimos atrás que el organismo no toma sino el exígeno que necesita. Vimos también que a causa del enrarecimiento del aire, el habitante de la altiplanicie de Bogotá no toma en los 21.91 litros, los 31.30 gramos que se toman a nivel del mar, en el mismo volumen.

Lo primero que se ocurre es que los habitantes de la altiplanicie suplen con una mayor capacidad torácica esta insuficiencia de oxígeno atmosférico; que introduciendo en cada inspiración un mayor volumen de gas, llega a absorber los mismos 31.30 gramos de exígeno por hora. Pero en 54 capacidades torácicas que he tomado en hombres, he hallado un promedio que alcanza a 1.8, cifra muy semejante a la que encontró el Dr. Corpas (1.7). El problema se reduce entonces a averiguar cuántas respiraciones se necesitan en Bogotá para tomar la cantidad de oxígeno indicada en peso. He aquí como lo resuelve el Dr. Corpas:

Según los experimentos de Bruner y Valentín, el hombre toma la cuarta parte del oxígeno que pasa por sus pulmones; de modo que para tomar los 31.30 gramos que necesita en cada hora, deben pasar por los pulmones, 125.20 gramos que están contenidos, a nivel del mar, en 450 litros de aire. Ahora bien: si en Bogotá contiene un litro de aire, 0.192 gramo de exígeno, los 125.20 gramos estarán contenidos en 652 litros de aire, que servirán, a razón de 500 c. c. por cada respiración, para 1,304 respiraciones por hora, o sea 21.7 por minuto.

Como resultado de 100 observaciones, el mismo autor encuentra, como término medio, 20.9 respiraciones por minuto. Como se ve, los dos resultados (el del cálculo y el de la observación), son sensiblemente iguales y se acercan también a la cifra de 20.3, fijada por el Dr. Coindet en la Mesa de Anáhuac.

Según el mismo autor, el número de pulsaciones por minuto es, en la altiplanicie, de 83. De modo que si no hay un mecanismo conpensador respecto a una mayor superficie de hemoglobina, lo hay por una mayor rapidez en la renovación de las superficies puestas en contacto para tomar el exígeno que debe ir a producir las combustiones. Lo difícil es saber si este mecanismo alcanza a suplir a aquél; si lo que resulta por el cálculo matemático, resulta también en cuanto a la práctica de las combustiones orgánicas, o si en definitiva la falta de superficie hemoglobínica es una de las causas de la baja de la temperatura animal en la altiplanicie.

Según mis observaciones tomadas en Tunja, no se llega a los mismos resultados.

Vimos atrás que la temperatura humana me da un promedio de 36.24, es decir, inferior al obtenido por los Drs. Pabón y Corpas en Bogotá. Ahora bien, estando esta última población colocada a un nivel inferior al de Tunja, debería encontrarse

en esta una polipnea compensadora y una mayor frecuencia del pulso; no sucede así, sin embargo, sino todo lo contrario, pues como se ve, mis promedios de 76 pulsaciones y de 20 respiraciones, son inferiores a los obtenidos en Bogotá por Corpas.

Si no fuera porque el número de observaciones es todavía insuficiente para sentar una conclusión definitiva, podríamos deducir (agregando estos dos datos al de la disminución del valor globular con la mayor altura) que nuestra raza, debido a múltiples circunstancias que enumeraré al final de este estudio, está atacada de un principio de degeneración fisiológica que la incapacita para defenderse contra las agresiones de la altura.

Ya se vió cómo la intensidad de las combustiones orgánicas está en razón directa de la cantidad de alimentos ingeridos, de modo que para compensar las pérdidas de calor que el organismo sufre en la altiplanicie por efecto de la altura, del estado higrométrico, de la temperatura ambiente, etc., se necesita agregar a los medios de defensa de que ya se ha hablado, el de una alimentación muy rica en materiales nutritivos.

Me extendería demasiado si me pusiera a relatar los experimentos que se han hecho sobre esta cuestión del alimento, como medio de defensa contra las causas de enfriamiento, tales como los de Levy, en perros,[1] las de Viault, en el hombre, las de Richet, en curíes,[2] las de Atwater y las de Rübner sobre el valor nutritivo de los alimentos.[3]

Estas consideraciones, agregadas a que la observación diaria y la tesis del Dr. Del Río [4] dejan comprender que hay una insuficiencia de eliminación de la urea entre nosotros, me condujeron a hacer investigaciones sobre la alimentación y luego sobre la eliminación azoada de la altiplanicie. En los capítulos siguientes se verá el resultado de estas investigaciones.

LOS ALIMENTOS.

En el capítulo anterior se hizo el análisis de uno de los elementos de combustión, o sea el oxígeno. En el presente voy a hacer algunas observaciones sobre el otro elemento, o sea el combustible.

Ya se ha visto que la calidad de los alimentos influye poderosamente en la intensidad de las combustiones orgánicas. Y como, por otra parte, se sabe que las materias alimenticias tienen composiciones distintas según la zona a que pertenecen, había pensado que la insuficiencia de eliminación de la urea que se nota entre nosotros, pudiera ser debida a una insuficiencia de materiales azoados en la alimentación. Venían en apoyo de esta hipótesis la consideración de que, por una parte, el aire de las alturas no tiene la misma cantidad de ázoe, en peso, que a nivel del mar, y por otra que no estando nuestro suelo científicamente abonado para la agricultura, pudiera adolecer de una nitrificación insuficiente. De modo que el alimento vegetal, origen de todos los materiales alimenticios (vease página 53), resultaría con una cantidad de ázoe insuficiente para abastecer a las necesidades del organismo, tal como sucede a los cereales de Egipto, por ejemplo.

Es verdad que el estudio de la eliminación azoada da datos suficientes para juzgar de la alimentación azoada, pero las consideraciones anteriores me han obligado a agregar este capítulo a manera de contra prueba.

Los análisis no solamente se han referido a las materias azoadas, sino a otras materias, cuya determinación puede ser de grande utilidad. Debo confesar que el número de análisis no ha sido suficiente para sacar conclusiones a este respecto; la falta de tiempo para extender más este trabajo y mi impericia en estos asuntos (que hizo que los primeros análisis fracasaran por una mala técnica) me impidieron hacerlos más numerosos, pero los pocos que voy a presentar, servirán a lo menos, para dar idea del poder nutritivo de nuestras materias alimenticias.

Las materias que he analizado son las que, en mi concepto, forman la base de nuestra alimentación: trigo, maíz, arvejas, habas, papas, arroz, carne y leche. Los análisis

[1] Lambling, loc. cit.
[2] Ch. Richet, Chaleur animale.
[3] Labbé, Les régimes alimentaires.
[4] Anastasio del Río. Tesis para el doctorado, Bogotá, 1892.

versan sobre los siguientes datos: agua, sales minerales, materias azoadas, materias grasas y materias azucaradas.

TÉCNICA DE LOS ANÁLISIS,

I. *Preparación de las muestras.*—La pulverización de los granos y demás materias destinadas al análisis, se ha hecho en un pequeño molino de discos de acero, acanalados. El producto del primer paso se remuele varias veces hasta obtener un polvo homogéneo.

II. *Dosado del agua.*—Se pesan en una balanza de precisión, en una cápsula previamente tarada, una cantidad cualquiera de la sustancia que se va a analizar (5 gramos por ejemplo) se lleva luego a la estufa a unos 100° y se mantiene allí durante 24 horas; se vuelve a pesar al cabo de este tiempo y la diferencia da el agua.

III. *Cenizas o sales minerales.*—La cápsula que sirvió para dosar el agua se pone sobre una parrilla, y con la ayuda de un soplete de gasolina se incinera hasta que no queden rastros de carbón. Se pesa, y el resultado, menos el peso de la cápsula da las cenizas.

IV. *Materias azoadas.*—Balland [1] aconseja el método de Kgedahl, basado en que las sustancias azoadas, calentadas, en presencia del ácido sulfúrico concentrado, se descomponen en ácido carbónico, agua y amoniaco. Todo el ázoe pasa al estado de amoniaco, y después, al combinarse con el ácido sulfúrico, forman sulfato de amoniaco. Basta descomponer, por un álcali, la sal formada; separar el amoniaco por destilación y dosalarlo volumétricamente.

Para esto se pone en un matraz de 500 c. c. de capacidad, 1 gr. de la materia que hay que analizar, 10 c. c. de solución al 30 por ciento de oxalato neutro de potasio y 10 c. c. de ácido sulfúrico concentrado. Se calienta el matraz directamente, si es de vidrio de Jena, o si no, interponiéndole una malla de alambre por medio de un reverbero Juwel u otro semejante.

El calentamiento debe ser moderado al principio, teniendo cuidado de agregar unos 15 c. c. de alcohol, cuando la espuma que se forme alcance a llenar las dos terceras partes del globo. Una vez que baje la espuma se aumenta la llama y se coloca entre el cuello del frasco un embudo, que tiene por objeto evitar que se escapen muchos vapores e indicar la presencia del vapor de agua por el ruido particular que produce al condensarse y caer sobre el fondo del globo; cuando se ha escapado todo este vapor, se regula la llama de modo de obtener una ebullición tranquila. Los vapores de ácido sulfuroso y de ácido sulfúrico se escapan entonces y producen una irritación muy molesta en las mucosas de las vías respiratorias. Cuando el líquido se descolora completamente o queda con un tinte ligeramente ambarino (esto sucede una o dos horas después de principiada la operación), se le quita la llama y se deja enfriar. Una vez enfriado el matraz, se agregan unos 30 ó 40 c. c. de agua tibia y luego se alcaliza con lejía de soda, hasta coloración rosada bien marcada de la fenoltaleina.

Después se pone todo el líquido en un globo que está en comunicación con un aparato destilador. El líquido destilado se recibe en un matraz donde hay unos 50 c. c. de ácido sulfúrico decinormal. Cuando el líquido destilado no coloree una gota de reactivo de Nesler (yodo-mercuriato de potasio), se suspende la operación.

Después de agregar unas gotas de fenoltaleina, se dosa por medio de soda decenormal, la cantidad de ácido que ha quedado libre y de este dato se deduce la cantidad de amoniaco desprendido. Sea n el número de centímetros cúbicos de soda empleados. La diferencia $50 - n$ es igual al amoniaco, y ésta multiplicada por 0.0014, da al ázoe de 1 gramo de sustancia, el cual multiplicado por 6.25 da la cantidad da materia albuminoidea.

[1] Balland, Les aliments, página 2, 1907.

Este procedimiento es mejor que el primitivo de Kgeldahl, que consiste en poner mercurio en vez de oxalato neutro, "porque el mercurio forma combinaciones amoniaco-mercúricas difíciles de descomponer que impedirán la libre destilación del amoniaco." Para impedir que estas combinaciones se formen, se agrega, después del enfriamiento del matraz en que se ha verificado la reacción, monosulfuro o hipofosfito de sodio, sustancias que son muy difíciles de conseguir, o de conseguir puras en el comercio.

Por vía de ensayo he hecho comparativamente la descomposición del sulfato de amoniaco y dosado del ázoe por este método de destilación y por el método volumétrico de Deniges, del cual hablaré al estudiar el dosado del ázoe total en la orina; sólo me han dado diferencias que no merecen tenerse en cuenta si se considera la simplificación que sufre el procedimiento.

Pero todos estos procedimientos adolecen del error de dosar las materias albuminoideas por el ázoe; y ya se dijo que hay en los vegetales cuerpos azoados que no son albuminoideos y que hay materias albuminoideas que contienen más de 16 por ciento de ázoe.

V. Materias grasas.—Este dosado se ha hecho agotando por el éter dos gramos de la sustancia en un aparato semejante al de Soxhlet, construído por el Dr. Eduardo Lleras Codazzi.

La sustancia se coloca en un papel de filtro previamente humedecido con alcohol. Encima del tubo que la contiene y en comunicación con él, hay un refrigerador, y debajo—también en comunicación—hay un globito previamente tarado, que contiene unos 5 c. c. de éter sulfúrico o de éter de petróleo. Se calienta el globito, y el éter, al evaporarse, disuelve la materia grasa, se condensa en el refrigerador y vuelve a caer al globo. Esta operación, se continúa por una hora, poco más o menos, teniendo cuidado de no calentar demasiado para que no se escape el éter.

El globo es colocado en la estufa a unos 100°, y después de unas veinticuatro horas, cuando se haya evaporado todo el éter, se pesa. El resultado, menos el peso del globo, da el peso de la materia grasa contenida en dos gramos de la sustancia que se analiza.

VI. Materias azucaradas.—Se agotan por el agua 5 gramos de materia, se hace hervir el agua de los lavados, filtrados con algunas gotas de ácido clorhídrico. Se defeca después por el subacetato de plomo en ligero exceso. Se filtra, y después de eliminar el exceso de plomo por fosfato o carbonato de sodio se vuelve a filtrar. Se lleva después a un volumen determinado, y se dosa el azúcar por los procedimientos ordinarios, con licor de Pasteur.

Para la leche: para el análisis de la leche estos métodos tienen ligeras variaciones. El estracto seco se dosa sobre 1 c. c. Las cenizas, sobre 5 c. c. previamente secadas a la estufa.

La lactosa sobre 5 c. c. a los cuales se agrega poco a poco 5 c. c. de alcohol a 65°, adicionado de 1 por 1,000 de ácido acético. Se lleva en seguida sobre un filtro previamente tarado. El coágulo que quede se lava con alcohol, y el líquido filtrado se lleva a un volumen determinado y en él se dosa la lactosa por el licor de Pasteur.[1] En el coágulo que queda en el filtro se dosa la materia grasa; después de extraída ésta, se pesa y el resultado, menos el peso del filtro y el de las sales, da la caseina.

Estos últimos procedimientos son los que emplea el Dr. Eduardo Lleras Codazzi, químico ayudante en el Laboratorio Municipal, a quien me tocó reemplazar durante varios meses.

La carne: En la carne que es otro de los alimentos animales que he analizado, sólo he dosado las materias albuminoideas sobre 2 gramos de sustancia.

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[1] Para el efecto de dosar la lactosa debe tenerse en cuenta que 5 gramos de glucosa equivalen a 6.75 de lactosa.

RESULTADOS.

	Muestras.		
	Núm. 1.	Núm. 2.	Núm. 3.
I. TRIGO.	*Porciento.*	*Porciento.*	*Porciento.*
Agua	11.10	11.20	11.20
Sales minerales	1.90	1.80	1.58
Materia grasa	1.95	2.00	2.19
Materias azoadas	9.80	12.82	11.10
Azúcares	2.50	2.60	1.55

	Muestras.			
	Núm. 1.	Núm. 2.	Núm. 3.	Núm. 4.
II. MAÍZ BLANCO.	*Porciento.*	*Porciento.*	*Porciento.*	*Porciento.*
Agua	12.00	11.90	12.10	12.00
Sales minerales	1.70	1.90	0.98	1.65
Materia grasa	3.90	3.90	4.85	5.10
Materias azoadas	11.10	8.64	13.58	12.25
Azúcares	2.40	1.56	1.80	1.90

	Muestras.	
	Núm. 1.	Núm. 2.
III. ARVEJAS.	*Porciento.*	*Porciento.*
Agua	12.20	14.98
Sales minerales	3.24	3.40
Materia grasa	.95	1.50
Materias azoadas	20.26	20.05
Azúcares	3.46	2.27
IV. HABAS.		
Agua	13.98	13.50
Sales minerales	2.40	2.24
Materia grasa	.98	1.25
Materias azoadas	21.78	20.40
Azúcares	3.46	3.10

	Muestras.	
	Norte-americano.	Del país.
V. ARROZ.	*Porciento.*	*Porciento.*
Agua	8	7.32
Sales minerales	1.19	.90
Materia grasa	1.60	1.50
Materias azoadas	7.564	9.264
Azúcares	.145	2
VI. PAPAS.	Núm. 1	
Materia grasa	1	.....
Materias azoadas	1.74	.....
Azúcares	20	.....

	Muestras.	
	Núm. 1.	Núm. 2.
VII. CARNE DESENGRASADA.	*Porciento.*	*Porciento.*
Materias azoadas	22.50	22.48

	Muestras.					
	Núm. 1.	Núm. 2.	Núm. 3.	Núm. 4.	Núm. 5.	Núm. 6.
VIII. LECHE.	*Por mil.*	*Por mil.*	*Por mil.*	*Por mil.*	*Por mil.*	*Por mil.*
Mantequilla	30	33	34	31	30	32
Lactosa	45	44	43	42	47	47
Sales	7	7.3	7.2	7.1	7	7
Caseína	46	39	41	42	36	37
Extracto seco	128	123	125	120	120	123
Reacción	Anf.	Anf.	Anf.	Anf.	Anf.	Anf.
Densidad	1,030	1,031	1,032	1,032	1,031	1,032

Si se comparan los análisis anteriores con los practicados en otros países, se verá que mis sospechas, respecto a la insuficiencia de materiales nutritivos y especialmente de materiales azoados en nuestros alimentos, eran infundadas. Voy a trascribir algunos de estos análisis, para que se pueda establecer la comparación:

Trigos de los Estados Unidos.—Estos tienen una composición muy variada, a causa de la diferencia de climas. En los trigos de Francia las diferencias son menos marcadas. He aquí los datos que suministra Balland:[1]

	Trigos de los Estados Unidos.		Trigos de Francia.	
	Máximum.	Mínimum.	Mínimum.	Máximum.
Agua	14.56	10.30	10.10	15.90
Materias azoadas	13.96	7.48	7.58	12.00
Grasas	2.25	1.10	1.10	2.00
Cenizas	1.98	1.42	1.12	2.10

Como se ve por estos pocos datos comparativos y por el resultado del análisis de las dos muestras de arroz, la una norteamericana y la otra del país, habría mas bien razón para pensar que nuestro suelo es suficientemente rico en materiales nutritivos y que nuestros productos alimenticios nada tienen que envidiar a los de la zona templada.

Hasta las mismas leguminosas que toman el ázoe [2] de la atmósfera, ázoe que, como se sabe, es insuficiente en las alturas, parece que dispusieran de un mecanismo compensador, análogo al de los animales para el oxígeno, porque su proporción de ázoe está en nuestras habas y en nuestras arvejas en la misma proporción que en Europa. Pero repito que el número de mis análisis ha sido muy pequeño, y que, por consiguiente, no pueden hacerse sobre ellos sino meras suposiciones.

Los análisis de eliminación azoada que se refieren a observaciones más numerosas, compensan, en parte, las deficiencias de aquellos.

ELIMINACIÓN AZOADA-GENERALIDADES.

Si se exceptúa una pequeña cantidad de ázoe, que proviene de la desintegración de ciertos elementos no albuminoideos de la alimentación vegetal, todo el ázoe que elimina el organismo, proviene de las materias proteicas.

Resumiré en el presente capítulo algunas generalidades sobre eliminación azoada, acompañándolas de distintas opiniones de autores extranjeros, a fin de que se puedan apreciar mejor los datos que daré en el capítulo siguiente, sobre la eliminación azoada en la altiplanicie.

[1] Balland, Loc. cit.

[2] Recherches sur la fijation de l'azote par les plantes. Anales l'Institut Pasteur, 1892, Núm. 2; —A. Balland, Loc. cit., págs. 99 y 100.

Ya se dijo que fué Liebig quien descubrió que las albuminoideas tienen ázoe y quien sugirió la idea de que la cantidad de ázoe eliminado podría ser proporcional a la cantidad de albúminas destruídas en el organismo; más tarde Bidder y Schmidt iniciaron experimentos sobre este asunto.

La molécula albuminoidea sufre en el organismo un estado tan avanzado de demoliciones, que siendo su peso molecular primitivo de 500 a 600, termina en cuerpos, como la urea, cuyo peso molecular es igual a 60. Es verdad que la urea no es el único producto de trasformación de las materias proteicas, pues hay otros de peso molecular más elevado; sin embargo, la nutrición es más perfecta cuanto más completamente se trasforme la albúmina en urea.

Parece que la mayor parte de las albuminoideas se destruyen en el organismo por hidratación, como in vitro bajo la acción de las diastasas proteicas o de los ácidos fuertes, es decir, que se fragmentan suministrando ácidos aminados, glicocola, leucina, alamina, etc., que son oxidados en seguida. En efecto, los fermentos proteolíticos que se han encontrado en los jugos de expresión de los tejidos desdoblan las proteicas, a la manera de la tripsina y hacen ácidos mono y diaminados; por otra parte, estos ácidos diaminados han sido encontrados en los líquidos del organismo y en los órganos mismos (glicocola en la orina y en la bilis, taurina que proviene de la cistina en la bilis, arginina en el bazo, etc.) ¿Qué se hacen entonces estos ácidos aminados? Sufren verdaderamente la desamidación en el lugar. En el curso de la autolisis del hígado y de otros órganos, los ácidos aminados agregados a los tejidos pierden su grupo AzH^2 al estado de AzH^3. Se sabe, además, que la alanina ingerida es trasformada en ácido láctico; después de la separación de su grupo AzH^2 al estado de AzH^3 el amoníaco es al punto trasformado en urea, que se elimina rápidamente mientras que el ácido desaminado es quemado más lentamente. (Magnus Levy.) La desasimilación de las albuminoideas se haría, pues, por etapas: (1) Desdoblamiento en ácidos aminados; (2) Desamidación de los ácidos aminados y trasformación del amoniaco en urea. (3) Oxidación del ácido desaminado.

Pero puede suceder que esta dislocación no sea completa y que una fracción de albúmina se escape; se ha pensado, en vista de la presencia de gruesas moléculas azoadas en la orina, que éstas representarían fragmentos ligeramente oxidados, sin haber sido previamente divididas, como las que resultan de la hidrolisis por acción diastásica.[1]

La trasformación que lleva la molécula albuminoidea hasta el conjunto de despojos eliminables, y en especial hasta la urea, se cumple muy rápidamente. Hacia la séptima hora después de las comidas alcanza su máximun, y entre la novena y la duodécima, ha terminado su eliminación.

La eliminación de los productos no azoados de la trasformación de las albuminoideas (ácido carbónico y agua), se verifica por la vía pulmonar.

La gran vía de la eliminación de los productos azoados es la orina, pues la excreción por el tubo digestivo no representa sino un 2 por ciento del ázoe total perdido por el organismo; las otras pérdidas son todavía más pequeñas, de aquí que casi todos los experimentadores no hayan tenido en cuenta sino la eliminación urinaria para medir la eliminación azoada.

Ázoe total.—En 99 adultos que eligen libremente su ración, Pluyer, Bleitien y Blilaud, han encontrado en la orina de las 24 horas 14.95 gramos, por término medio, de ázoe total, o 0.227 gramos por kilogramo de peso vivo, lo que corresponde a un consumo de 96.467 gramos de albúmina, o 1.464 gramos por kilo de peso vivo; para los individuos jóvenes bien alimentados que no suministran sino un trabajo mecánico mediocre, la excreción azoada de las 24 horas fué de 14.37 gramos, que indica la destrucción de 93.7 de albumina. En fin, en 27 individuos que suministraban un trabajo considerable, el ázoe total se elevó a 16.68 gramos, o sea 0.249 gramos por kilo de peso vivo, lo que da una destrucción de albúmina de 107.60 gramos o 1.688 gramos por kilo de peso vivo por día.[2]

Lambling cree que en Francia no se puede adoptar como término medio los números que se acaban de leer, los cuales son, en su concepto, demasiado elevados. El deter-

[1] Gley, Physiologie, 1910.

[2] Para comprender esta relación véase página —.

minó sobre 79 sujetos de la clase media de Lille y de los alrededores, donde, según dice, es general la costumbre de las grandes comidas, una cantidad total de 13.91 gramos en los hombres (50 sujetos) y de 11.74 gramos en las mujeres (29 sujetos) para el período de las 24 horas; la alimentación era elegida libremente. Sin embargo, se verá adelante por los análisis hechos últimamente en Francia que esta cifra es muy superior a las que da Lambling.

La repartición del ázoe en las orinas, en caso de alimentación mixta, es, poco más o menos, la siguiente, según el mismo autor:

En urea, 84 a 87 por ciento. En amoniaco, 2 a 5 por ciento. En ácido úrico, 2 a 3 por ciento. En materias extractivas azoadas, 7 a 10 por ciento.

Estos números varían en límites muy extensos, cuando se pasa de la alimentación vegetal a la alimentación animal, como se verá por el cuadro siguiente:[1]

	Régimen mixto.	Régimen animal.	Régimen vegetal.
Urea	85.1 (de 82.9 a 87.3)	86.8 (de 79.2 a 88.2)	80.5 (de 76.9 a 83.4)
Amoníaco	4.59 (de 3.8 a 5.8)	4.84 (de 3.5 a 5.6)	4.29 (de 3.4 a 8.6)
Otros materiales azoados	10.36 (de 8 a 11.9)	8.39 (de 11 a 8.2)	15.7 (de 10.5 a 17.6)

Khegnie ha notado que cuando se da pan a un perro, la secreción gástrica es más abundante que cuando se le da leche. Partiendo de este hecho, Rjasawzeff ha suministrado a un perro la misma cantidad de ázoe (4 gramos) primero en forma de pan y luego en la de leche; la cifra de la excreción azoada fué, en el ensayo del pan dos o tres yeces mayor que en el ensayo de la leche. Parece, pues, que existe una relación directa entre la intensidad del trabajo secretor impuesto al estómago y la cantidad de despojos azoados. El trabajo de secreción del tubo digestivo, sería, según esto, una de las causas de la necesidad de albúmina.

Las observaciones sobre eliminación azoada deben referirse de preferencia a la urea, el amoníaco, el ácido úrico y las bases púricas, el ázoe de las bases precipitables por el ácido sflicotúngstíco, y además diferentes relaciones de estos elementos entre sí y con otros materiales de eliminación urinaria. Para comprender su importancia, es preciso hacer el resumen del origen de cada uno de ellos.

Urea.—La doctrina de la combustión hacía considerar la urea como resultado de la oxidación de las albuminoideas, a pesar de la imposibilidad de producir la in vitro por medio de los cuerpos oxidantes, pero en 1856, Beauchamp pareció haber llenado definitivamente este vacío con el descubrimiento de la producción in vitros de pequeñas cantidades de urea por la oxidación de las materias albuminoideas, en presencia del permangamato de potasio. Al año siguiente Saedeler y luego Subbotise objetaron las conclusiones de Beauchamp. El debate, planteado nuevamente por una publicación de Beauchamp y de Ritter, fué luego considerado definitivamente cerrado por los resultados negativos de Laen y de Tapeiner.

Se empezó luego a dar grande importancia a las reacciones orgánicas de desdoblamiento y de hidratación, y bajo la influencia de los trabajos de Schutzemberger, referentes al desdoblamiento de la albúmina en presencia del hidrato de barita, se llegó a considerar la urea como proveniente de las albuminoideas por simple hidrolisis. Sobre este punto los trabajos de Schutzemberger han sido confirmados por los de Drechsel, quien ha podido separar de la caseina, por medio del ácido clorhídrico, hirviendo, bases azoadas complejas: la lisina y la lisalinina que el agua de barita desdobla en caliente con producción de urea. Por otra parte, la arginina, una de las bases exónicas, suministrada por la hidrolisis de las albuminoideas, es igualmente desdoblada por la barita con formación de urea. Pero Drechsel reconoció, al mismo tiempo, que de esta manera no se explicaba sino la formación de una pequeña cantidad de urea en el organismo. En efecto, en los experimentos de Schutzemberger la

[1] Gulmlich.

albúmina es desdoblada en urea y oxiamida (o más exactamente, en ácido carbónico y amoníaco en las proporciones de la urea y de la oxiamida), por una parte, y por otra, en una mezcla de ácidos aminados. Se puede calcular que la urea así separada por hidrolisis, no representa sino, aproximadamente, un 10 por ciento del ázoe total y que sólo los ácidos aminados representan el 75 por ciento del ázoe de la molécula albuminoidea, de donde se deduce que otros fenómenos, fuera de la hidrolisis, intervienen en la formación de la urea.

Por los experimentos clásicos de Schultzen y Nenki, se sabía desde 1867, que estos ácidos aminados pueden constituir un producto hacia la urea: la glicocola, la leucina, ingeridas, se trasforman íntegramente en urea; en esta observación Von Kmerin comprendió el ácido aspártico. Pero hay que notar que los ácidos aminados no tienen sino un solo átomo de Az, y la urea tiene dos; es necesario admitir entonces la fijación de otro resto de Az. Schultzen y Nenki habían pensado en el ácido ciánico y Salkowski demostró que una parte de dicho ácido se fija fácilmente in vitro sobre los ácidos aminados, para dar lugar a uramidos, que son en realidad ureas sustituidas, y que, por otra parte, en el organismo muchos ácidos aminados se trasforman en ácidos uramídicos por fijación de ácido ciánico Es este el punto de partida de otra teoría de formación de la urea; la teoría del ácido ciánico, que explica la formación de la urea por síntesis, semejante a la síntesis histórica de la urea por Woehler, por medio del ácido ciánico y el amoniaco. Esta teoría, desarrollada sobre todo por Hoppe Seyler, no tiene base experimental directa en el sentido de que jamás se ha logrado aislar el término ciánico como punto de partida de toda constitución.

He aquí, según Gley, los mecanismos por los cuales los ácidos aminados suministran urea:

I. Ya se vió que se han encontrado en todos los órganos, y principalmente en el hígado, diastasas que separan el ázoe de los ácidos aminados bajo la forma de amoníaco. Esta desamidación comprende, pues, ázoe del aminoácido, el cual queda desde entonces reducido a la condición de un simple ácido graso, cuyo destino se confunde con el de los ácidos grasos y las grasas. En cuanto al amoniaco producido, va a engendrar urea, uniéndose, según Schmildeberg, con el ácido carbónico y dejando agua en libertad:

Urea: $$2AzH_3+CO_2=CO\begin{matrix}AzH_2\\AzH_2\end{matrix}+OH^2O$$

Según otros la urea se deriva del carbonato de amoníaco, previamente formado:

$$CO\begin{matrix}AzH^4\\AzH^4\end{matrix}=CO\begin{matrix}AzH^2\\AzH^2\end{matrix}+H^4O$$

En los dos casos hay síntesis total de urea con deshidratación.

II. Por otra parte, se ha obtenido in vitro carbamato de amonio por oxidación de los ácidos aminados. Es, pues, posible que estos den por oxidación en el hígado, carbamato, de donde proviene en seguida la urea por deshidratación:

$$CO\frac{AzH^4}{AzH_2}-H_2O=CO\begin{matrix}AzH_2\\AzH_2\end{matrix}$$

Podría suceder también que sobre el grupo $COAz\,H_2$ de un aminoácido se fijara otro AzH_2 y que por una oxidación concomitante se formara urea (síntesis parcial con oxidación). Se ha mostrado, por ejemplo, que el oxiamato de sodio da in vitro urea oxidándolo por el permanganato de potasio.

Lambling da grande importancia a la primera de estas teorías (formación de la urea por combinación de ácido carbónico con el amoníaco dejando el agua en libertad) la cual ha llamado la atención, dirigido los esfuerzos de los experimentadores y tiene en su favor la explicación de hechos muy trascendentales, a saber:

1. En los herbívoros, la ingestión de las sales amoniacales, sean de ácidos fuertes, como el cloruro de amonio, o de ácidos orgánicos combustibles, como el citrato, es

seguida de un aumento de la urea excretada. En los carnívoros y en el hombre este mismo resultado no es obtenido claramente sino con las sales amoniacales de ácidos orgánicos, como el carbonato de amoníaco. La razón de esta diferencia se verá más adelante.

Esta teoría y los dos órdenes de hechos que se acaban de señalar, encuentran una verificación notable en una serie de fenómenos relativos a la acción de los ácidos sobre la excreción de la urea, y del amoníaco. Si el amoníaco y el ácido carbónico son realmente los precursores de la urea, la presencia de los ácidos fuertes—es decir de cuerpos capaces de fijar sólidamente el amoníaco—debe impedir la formación de la urea y aumentar la proporción de sales amoniacales en la orina, esto es lo que la experiencia demuestra claramente.

2. Se ha visto, en efecto, que en el carnívoro el carbonato de amoníaco ingerido pasa en la orina al estado de urea; el cloruro de amonio pasa inalterado a la orina, porque el amoníaco, fuertemente retenido por el ácido clorhídrico no puede entrar en reacción con el ácido carbónico. Si en el herbívoro el cloruro de amonio contribuye a la formación de la urea, esto se debe a que la alimentación vegetal lleva consigo una superabundancia de bases alcalinas que transformadas en el organismo en carbonato de potasio o de sodio, hacen la doble descomposición con el cloruro de amonio y le transforman en carbonato.

3. Además, en el perro y en el hombre la ingestión de ácidos minerales aumenta la cantidad de amoníaco de las orinas y disminuye la de la urea porque el ácido introducido fija y retiene fuertemente el amoníaco.

Inversamente, la ingestión de álcalis en el hombre, reduce al mínimum la excreción de las sales amoniacales.

Esta neutralización de los ácidos por el amoníaco, así sustraído al proceso formador de la urea, constituye el mecanismo por el cual el organismo de los carnívoros, o del hombre, resiste la intoxicación por los ácidos y preserva de los accidentes graves que se producirían si las bases necesarias para el funcionamiento normal de los protoplasmas vinieran a ser arrancadas a las células.

En los herbívoros este mecanismo regulador no existe. Así se ve que en esos animales la intoxicación por los ácidos termina rápidamente en accidentes mortales.

Los ácidos que se forman en el organismo, en el curso mismo de la desasimilación, producen los mismos efectos que si fueran introducidos experimentalmente. Como estos ácidos resultan, sobre todo, de la desagregación de las albúminas, se ve, en lo que concierne a la excreción del amoníaco, que la alimentación animal obra como la ingestión de ácidos, y la vegetal, como la de álcalis. Así, Caranda ha encontrado en sí mismo, para una alimentación vegetal, 0 grms. 0.3998 de amoníaco por día; para una alimentación, sobre todo, animal, grms. 0.875, y para una alimentación mixta, grms. 0.6422.

La inanición (que es una alimentación animal) y el ejercicio (que disminuye la alcalinidad de la sangre) producen un aumento de la excreción del amoníaco, el que se ha visto llegar, en la inanición, al 10 por ciento del ázoe total, en vez de 2 a 5 por ciento que es la suma normal.

4. Los estados patológicos, que causan un aumento de producción de ácidos en el organismo, aumentan la excreción del amoníaco por las orinas. En el curso de la diabetes y especialmente en el período de coma, la orina contiene proporciones considerables de amoníaco, de 3 a 6 gramos por día, y en un caso de Stadelmann, hasta de 12, en vez de 1 a 1.50, cifra normal. Este hecho es debido a la fundición rápida y anormal de los protoplasmas celulares y a la producción de cantidades considerables de ácidos anormales, tales como el ácido acetilacético y el ácido Boxibutírico, que inundan literalmente el organismo del diabético; y es precisamente después de haber notado la presencia de cantidades considerables de amoníaco en la orina de los diabéticos, cuando Stadelmann dedujo por este hecho una intoxicación ácida y encontró después el ácido Boxibutírico. Las cantidades de este ácido son frecuentemente,

en la orina de los diabéticos, de 30 a 50 gramos. Este grado de intoxicación ácida da, pues, la explicación de la amoniuria diabética.

Se sabe que estas reacciones, que dan lugar a la formación de urea, se verifican, casi en su totalidad, en el hígado.

Los experimentos por medio de los cuales se demuestra que este es el lugar de tal formación, son suficientemente conocidos, para no detenerme a relatarlos.

Amoniaco.—Al lado de la urea debe hacerse mención especial del amoniaco, que se encuentra siempre en la orina en pequeñas cantidades (1.11 gramos en 24 horas, según Maillard); esta cantidad representa la parte del amoniaco que no se ha empleado en la formación de la urea.

En sus investigaciones clásicas sobre los efectos de la fístula de Eck, Nenky y Pawloff han visto, con su colaborador Zaleski, que el hígado recibe por la vena porta, aproximadamente, 6.6 gramos de amoníaco por 100 c. c. de sangre; en la vena suprahepática no se encuentran más de 1.4 gramos, de donde se ha calculado, según la velocidad de la sangre al través del hígado, que este órgano retiene, en las 10 horas que siguen a una comida, en un perro 9.5 de kilos, aproximadamente, 5 gramos de amoníaco, lo que corresponde a más de 8 gramos de urea. Al hablar del origen de la urea se vió cual es el origen del amoníaco; se vió cómo y por qué la eliminación de las sales amoniacales aumenta o disminuye, según que la alimentación sea animal o vegetal, ácida o alcalina.

Más adelante hablaré del índice de imperfección urogenética de Maillard, basado sobre la relación entre el ázoe del amoníaco y éste, más el ázoe de la urea.

Acido úrico y bases púricas.—Las nucleo-proteidas constituyen un grupo muy importante. Son estas sustancias las que forman la mayor parte de los grupos celulares. No hay que confundirlas con las nucleo-albúminas o pseudonucleinas, entre las cuales se encuentran la vitelina y la caseina.

Como las nucleo-proteidas, las pseudo-nucleinas contienen fósforo, pero no encierran purinas; estos cuerpos parecen ser los característicos de las nucleo-proteidas, o a lo menos del ácido nucleínico que entra en su constitución.[1]

Las nucleo-proteidas son esencialmente formadas por la unión del ácido nucleínico con diferentes materias proteicas, y como estas son extremadamente variables, se concibe que las nuclo-proteidas sean muy numerosas.

Bajo la influencia de ciertos reactivos químicos por la acción del jugo gástrico en el organismo, las nucleo-proteidas abandonan un grupo proteico y queda un cuerpo llamado nucleina, que se descompone, a su turno, en albúmina y en ácido nucleico. Este último suministra cuatro especies de cuerpos: ácido fosfórico, derivados pirimídicos, bases xánticas e hidratos de carbono.

Pero algunas de las proteidas son más complejas de lo que indica esta fórmula; la nucleina, además de la albúmina y del ácido nucleico, puede contener hipoxantina y bases diferentes, tales como creatina, carnacina ignotina, novaina. Estos cuerpos, que no son unidos al ácido nucleico, son, sobre todo, abundantes en las nucleo-proteidas sacadas de los músculos.

En el tubo digestivo, las albúminas puestas en libertad por el jugo gástrico, son trasformadas, según el proceso habitual, por la clorhidro-pepsina, y en cuanto al ácido nucleínico, es descompuesto por un fermento, muy extendido en el organismo; la nucleasa, en sus componentes, que son: ácido fosfórico, un azúcar, adenina, guanina, citosina y elurina.

El ácido fosfórico, que es ácido ortofosfórico, proviene del ácido tímico, el cual encierra todo el fósforo de las nucleo-proteidas. El azúcar no es conocido sino por sus productos de desdoblamiento. La citosina y la timina, derivados primarios del ácido nucleico. La uracila es un derivado secundario. Estos tres últimos cuerpos son semejantes a la pirimidina.

Los cuerpos pirimidicos parecen muy inestables; en el organismo se destruyen rápidamente, abandonando ácido carbónico y urea.

[1] Prof. C. H. Rogert, Digestion et Nutrition. pág. 518, 1910.

Más importante es el estudio de la adenina y de la guanina. Estas dos sustancias pertenecen a las bases púricas, de las que hace también parte el ácido úrico.

Fué Fischer quien estableció la estructura definitiva de la purina. Todas pertenecen a una misma serie, que encierra este núcleo:

(1) Az—C (6)
(2) C (5)—Az (7)
C (8)
(3) Az—(4) C—Az (9)

La numeración que se ha adoptado[1] facilita el estudio de los derivados. Basta, en efecto, indicar para cada cuerpo el número correspondiente a los productos de sustitución, para comprender la posición exacta.

El compuesto hidrogenado fundamental ha recibido de Fischer el nombre de purina. Conociendo la constitución de éste, se puede comprender fácilmente cuál es la de los derivados.

(1) Az=CH (6) — AzH (7)

(2) HC—C (5) — CH (8)

(3) AzC (4) — Az (9)

Purina $C^5H^4-Az^4$

La adenina, por ejemplo, se llama (6) amido-purina, porque resulta de la sustitución del grupo (6) CH de la purina por un radical amido (AzH_2), de tal manera que la fórmula queda: $C_5H_5Az_5$.

De la misma manera se puede comprender, por el simple nombre, la constitución de todos los demás derivados; (6) oxipurina o hipoxantina, reemplazando un H del grupo 6 por un O ($C^5H^4Az^4O$) 2 amido, 6 oxipurina, o guanina ($C^5H^5Az^5O$)—2, 6 dioxipurina o xantina ($C^5H^4Az^4O^2$)—6 amido 2, 8 dioxipurina ($C^5H^5Az^5O^2$)—2, 6, 8 trioxipurina ($C^5H^4Az^4O^3$) ácido úrico, etc. Siguen luego haciendo las sustituciones los otros derivados metilados (monometilxantina, paraxantina, teobromina, teofilina' cafeina), cuyos nombres químicos no doy por no alargarme demasiado.

Las purinas del organismo provienen: (1) De la desintegración de las nucleoproteidas de los alimentos; (2) de la desintegración de las nucleo-proteidas de los tejidos. A estas dos fuentes hay que agregar una tercera: la que resulta de la introducción de derivados púricos, tales como teobromina, cafeina, etc., una parte de las cuales es eliminada por las orinas. Los fermentos que descompomen las nucleoproteidas y ponen el ácido nucléico en libertad, son abundantemente extendidos; pues no solamente los jugos digestivos, sino todos los órganos y tejidos, son capaces de producir tales desdoblamientos. Este es un proceso indispensable para el juego natural de la desasimilación.

El fermento que descompone el ácido nuclénico, la nucleasa, se encuentra en el timo, el bazo, el páncreas, la mucosa del intestino delgado, como también en los músculos, los glóbulos nucleados de las aves; en una palabra, la nucleasa existe donde quiera que existan nucleo-proteidas.

El jugo pancreático no descompone el ácido nucleínico; le hace solamente perder su carácter coloidal y lo vuelve dializable; es lo que algunos autores expresan diciendo que cambia el ácido nucleínico *a* en ácido nucleínico *b*. Esta trasformación permite al ácido nucleínico difundirse en la pared intestinal. Allí se encuentra con la nucleasa y a favor de esta acción pone en libertad sus diversos componentes.

El término último de la trasformación de las bases púricas es el ácido úrico, para lo cual interviene la acción sucesiva de dos especies de fermentos: uno desamidante y otro oxidante.

[1] Prof. C. H. Roger, Digestion et nutrition, pág. 521, 1910.

Los fermentos desamidantes trasforman la adenina y la guanina—o sean los productos primarios que provienen del ácido nucleínico—el primero en hipoxantina y el segundo en xantina. Un simple proceso de hidración da cuenta del fenónemo

Adenina. Hipoxantina.
$$C^5H^5Az^5+H^2O=C^5H^4Az^4O+AzH^3$$

Guanina. Xantina.
$$C^5H^5Az^5O+H^2O=C^5H^4Az^4O+AzH^3$$

Como se ve, el amido, que ocupa la posición 6 en la adenina y la posición 2 en la guanina, se elimina al estado de amoníaco.

Los fermentos desamidantes, adenasa y guanasa, descubiertos en el bazo, se encuentran en la mayor parte de los órganos.

Los fermentos oxidantes son también en número de dos: la xantoxidasa, que oxida la xantina y la trasforma en ácido úrico y la hipoxantidasa, que hace lo mismo con la hipoxantina. Estos fermentos oxidantes no son tan extendidos como los precedentes; se les encuentra solamente en el bazo, el hígado, el intestino, los riñones, los pulmones y los músculos.

Una parte del ácido úrico es trasformada en el hígado en urea, segun lo creen todavía algunos autores. Pero esto no quiere decir que, como se creía antiguamente, el ácido úrico sea un producto hacia la urea, pues ya que se conocen bien todas las trasformaciones de los nucleo-proteidos y las de las bases púricas, se ha visto que todos estos cuerpos terminan en el ácido úrico, que es el término final de la serie, como la urea es el término último de las trasformaciones que sufren las albúminas.[1] Esto me ha sugerido la idea de un nuevo coeficiente urológico, de que hablaré más adelante.

Ázoe silicotúngstico.—Se sabe que, además de los cuerpos azoados de función ácida, como el ácido úrico, o de función débilmente básica, como la urea, la orina encierra ciertas substancias suficientemente básicas para formar con el ácido silicotúngstico combinaciones muy poco solubles o prácticamente insolubles, análogas a las combinaciones silicotúngsticas alcalóidicas estudiadas por R. Godefoy y por G. Bertrand.

Un estudio cuantitativo de estas bases urinarias fué hecho por Guillemard,[2] quien encontró variaciones importantes, según el estado normal o patológico de los individuos, y diferencias apreciables según el sistema alimenticio. Posteriormente Maillard [3] hizo, a este respecto, observaciones muy interesantes y encontró una eliminación media de 0.60 c. c., en las 24 horas, de este ázoe que para abreviar se ha llamado incorrectamente ácido silicotúngstico, por ser este ácido el que sirve para precipitarlo.

De las relaciones urológicas hablaré en el capítulo siguiente.

Eliminación Azoada en la Altiplanicie—Procedimientos Empleados—Resultados Obtenidos.

Es el análisis químico de ias orinas, dice Marcel Labbé,[4] lo que suministra datos más numerosos y más precisos en el estudio de la nutrición. Desde la más remota antigüedad, los médicos lo han utilizado en la solución de los problemas más complicados. Los métodos, muy rudimentarios al principio, han ido perfeccionándose poco a poco.

La importancia de este estudio adquiere mayor interés desde que se trata de materiales azoados, puesto que, según se vió atrás, la gran vía de eliminación de estos productos es la orina.

Mis observaciones sobre esta materia se fundan sobre 96 análisis de orinas de individuos en estado fisiológico. Todos los sujetos fueron examinados previamente, y hasta donde es posible afirmar, después de un examen detenido, en ninguno de ellos se descubrió nada que hiciera pensar en una alteración de la salud. Hasta donde

[1] Roger, Loc. cit.
[2] Guillemard, Contribution à l'étude des alcaloides de l'urine, thèse de Paris, 1902.
[3] Maillard, Journ. de Phys. et de Pat. Gén., 15 nov. 908.-15 mars 1909.
[4] M. Labbé, Des régimes alimentaires.

me fué posible, vigilé la colección de las orinas, y a aquellos en quienes no se pudo verificar esta vigilancia, se les dieron las instrucciones necesarias a fin de que se recogieran con el mayor cuidado colectando orinas de las 24 horas, y nada más que las de las 24 horas.

Con tal objeto, las orinas se debían recoger en vasijas lo mejor lavadas que fuera posible. Una primera mixión sería ejecutada a una hora cualquiera, y de esa hora en adelante se empezaría a recoger la orina hasta el día siguiente a la misma hora, en que se recogería la última porción que hubiera en ese momento en la vejiga, teniendo cuidado de no dejar perder la que se emitiera durante las deposiciones.

Si se consideran las dificultades para conseguir orina en estas condiciones y si se tiene en cuenta que para hacer estos análisis tuve que empezar por preparar y titular desde el primero hasta el último de los reactivos, teniendo, algunas veces, que preparar materias primas que no se encuentran en Bogotá, se comprenderá por qué gasté una cantidad de tiempo increíble en verificar estos análisis y por qué no alcancé a llegar al número de 100, que me había fijado como mínimun cuando principié mis observaciones.

Las orinas de los análisis hechos en Bogotá, pertenecen, unas a obreros o a sirvientes, algunos de ellos asistentes del hospital y otras, las provenientes de la clase acomodada, pertenecen, en su mayor parte, a estudiantes y médicos y a algunos pocos comerciantes. Estas últimas fueron más escasas por la mayor dificultad para conseguirlas.

Los análisis de Tunja pertenecen muchos de ellos a individuos de clase social acomodada cuyas orinas he podido conseguir y recoger minuciosamente, como médico que soy de algunas compañías de seguros; otras de estas orinas pertenecen a soldados de la unidad del ejército que presta la guarnición en esta ciudad.

Estos últimos individuos están alimentados con el régimen que se indicará más adelante, régimen que por ser algo superior al usado generalmente por nuestras clases trabajadoras, no me ha parecido lógico incluir, por lo que a sus análisis de sus orinas respecta, entre estas.

Por esta circunstancia y por ser relativamente pequeño el número de mis observaciones de Tunja, he resuelto no dividir en dos partes los cuadros, como los de Bogotá, sino sacar un promedio general de todos ellos.

Métodos Empleados.

Los análisis de las orinas se han dirigido a los siguientes puntos: volumen de la orina emitida en 24 horas; densidad, acidez (expresada en hidrógeno), amoníaco, urea, purinas totales (expresadas en ácido úrico), ácido úrico, bases puricas (expresadas en xantina), ázoe total, ázoe amoniacal, ázoe de la urea, ázoe purico total, (núcleo purico solamente) ázoe del ácido úrico, ázoe de las bases puricas, anhídrido fosfórico para efectos de la relación atómica. P: Az. Relaciones urinarias.

Para investigar estos diversos elementos he querido emplear los métodos más exactos y al mismo tiempo los menos complicados. He aquí la descripción de ellos:

Acidez.—Siguiendo el precepto de Maillard respecto a la acidez de la orina, de que no hay método que no adolezca de empirismo, he resuelto emplear el método directo con fenoltaleina, porque según el mismo autor, no es menos bueno que los otros, y por que, según se verá más adelante, constituye la primera operación para la dosificación del amoníaco.

Se toman 10 c. c. de orina y se colocan en un globo aforado a 100 c. c. se completa el volumen hasta la línea del globo, con agua destilada. La mezcla se coloca en una fiola de Erlenmeyer y se le agregan unas tres o cuatro gotas de solución alcohólica de fenolteneina al 1 por ciento; después se vierte gota a gota, con una bureta de Gay Lisac, solución decinormal de soda hasta la aparición del tinte débilmente rosado.

Para obtener la acidez, en gramos, de hidrógeno por litro, se multiplica por 0.01 el número de c. c. que se hayan gastado de la solución de soda.[1]

[1] Algunos autores aconsejan agregar 6 grms. de oxalato de potasio para precipitar las sales de calcio las que obrarían sobre los fosfatos cuando se agrega la soda.

Azoe total.—El mismo procedimiento de Kjeldahl de que ya hablé atrás con algunas variaciones.

La reacción se efectúa con 20 c. c. de orina, 5 c. c. de solución al 30 por ciento de oxalato neutro de potasio y 5 c. c. de ácido sulfúrico puro. La espuma que se forma baja casi siempre espontáneamente y es raro que haya que agregar alcohol, como cuando se trata de materias alimenticias.

Una vez descolorado el líquido, se deja enfriar, como de costumbre, agregándole unos 30 c. c. de agua tibia.

Se pone luego unas gotas de solución de fenoltaleina y se agrega, gota a gota, una lejía de soda exenta de carbonato y de 1.15 de densidad, hasta que aparezca la coloración débilmente rosada; tan débilmente, que desaparezca con 3 ó 4 gotas de ácido sulfúrico al décimo; después se completa el volumen a 100 c. c. en un globo aforado.

Para averiguar la cantidad de ázoe en este licor, se opera por comparación con una solución titulada de cloruro de amonio, al 7.65 por ciento, de tal manera que 5 c. c. de esta solución, al descomponerse por el hipobromito de sodio, dan exactamente 0.1 gramo de ázoe. Se introducen, pues, en el ureómetro 5 c. c. de esta solución, como si se tratara de medir urea y luego se hace lo mismo con 5 c. c. del líquido que resulta de la reacción, que equivalen a 1 c. c. de orina. Una simple relación respecto a los volúmenes ocupados en cada operación por el ázoe desprendido, mostrará el ázoe contenido en 1 c. c. de orina.

Amoníaco.—Se sabe que todos los métodos que consisten en destilar la orina en presencia de álcalis, de cal o de magnesia, de carbonatos alcalinos o aún terrosos, dan resultados erróneos, por exceso, a causa de una hidrolisis parcial de la urea. Y no es verdad, según Maillard, que la destilación en presencia del carbonato de sodio o de magnesio en el vacío y a 45° o 50°, esté al abrigo de estas causas de error. Los otros métodos, si no son susceptibles de errores químicos, lo son de errores biológicos.

El método de Ronchese, uno de los más recientes, es justamente elogiado por Maillard, Jones y por Guiard y Grimbert;[1] tiene la inmensa ventaja de ser muy exacto, muy sencillo y muy rápido.

Se sabe, desde los trabajos de Detepine y de Cambier y Brodiet, que las sales amoniacales son trasformadas por al aldheida fórmica en sales de una nueva base, la exametileneamida; como esta no sufre la influencia de la fenoltaleina, los ácidos primitivamente combinados al amoníaco, se comportan con este indicador como si estuvieran libres; de modo que para encontrar la neutralidad a la fenoltaleina, previamente comprobada, hay que agregar una solución decinormal de soda, precisamente equivalente a la cantidad de amoníaco. Este método tiene además la inmensa ventaja de dosar al mismo tiempo los ácidos aminados.

Diez c. c. de orina se aumentan con agua destilada, recientemente hervida para que no contenga carbonatos, hasta completar el volumen de 100 c. c., y se neutraliza, como ya dije al hablar de la determinación de la acidez. Por otra parte, se neutralizan de la misma manera 20 c. c. de aldheida fórmica al 20 por ciento (formol del comercio diluído de su volumen de agua). Se mezclan entonces estas dos soluciones, y como se verifica entonces la reacción que pone en libertad los ácidos de las sales amoniacales, los líquidos pierden instantáneamente el color rosado. Basta entonces neutralizar de nuevo estos ácidos con soda decinormal, para saber la cantidad de amoniaco empleada en cada litro de orina, pues no hay sino que multiplicar por 0.17 el número de c. c. de solución de soda empleados. Pero como las sales amoniacales hacen retardar un poco la aparición del tinte rosado, hay que agregar 0.1 por cada 3 c. c. de soda gastados en la neutralización final.

Urea.—Maillard, en un trabajo citado antes, empleó para medir la urea en la orina, el método de Folin, que está fundado en la hidrolisis de la urea por el cloruro de magnesio, fundido a 160°. Se dosa luego el amoníaco por destilación sobre el ácido sulfúrico cuartonormal. Del resultado hay que deducir el amoníaco de la orina,

[1] Guiart, et Grimbert, Diagnostique chimique, 1912, Maillard, loc. cit.

previamente medido. L. G. de Saint-Martin prefiere al cloruro de magnesio el de litio. El método de la descomposición y dosado por la *ureasa* es bastante preciso aunque lento.

El dosado gasométrico ha sido objeto de graves críticas; sin embargo, estas críticas han sido quizá exageradas, como lo prueba la concordancia de los resultados obtenidos por Maillard y los obtenidos por Desgrez y Ayrignac.[1] En favor de la rehabilitación de este método está también la tesis de Ronchese.[2]

Resolví emplear el método gasométrico, porque si es verdad que adolece de muchos errores, ellos pueden corregirse fácilmente.

Este método está fundado en la descomposición de la urea por el hipobromito de soda, en ázoe, ácido carbónico y agua; el ácido carbónico es retenido, si se opera, con un exceso de soda, y el volumen del ázoe puesto en libertad es proporcional a la cantidad de urea contenida en la orina empleada.

Los aparatos destinados a medir el ázoe son muchos; yo empleé para estos análisis, como para el dosado del ázoe total, uno construido por el señor R. Ferreira, según el modelo de Mercier o del doctor Montoya, compuesto de un tubo en U, con un líquido en su interior y una de sus ramas en comunicación con un frasco donde se efectúa la reacción. La graduación es arbitraria, más adelante se comprenderá por qué. Las uniones son muy herméticas para evitar el menor escape de gas..

Uno de los inconvenientes de este método consiste en que los resultados son variables, como son variables la presión y la temperatura. Para subsanarlo se emplea una solución tenue de urea al 2 por mil (adicionada de unos 4 a 6 por 1,000 de fenol puro para asegurar su conservación) con la cual se hace un análisis, inmediatamente antes del de la orina. Sabiendo que 5 c. c. de la solución equivalen a 0.01 de urea, se puede, por cálculo, deducir la cantidad de urea contenida en el volumen de orina empleado. La corrección que se hace de esta manera respecto a la presión y a la temperatura es tan considerable, que sobre una misma orina hice el mismo análisis por el método de Folin y luego por el método gasométrico, operando comparativemente con la solución de urea en un aparato calculado para 0.560 c. c. de presión y 15° de temperatura, cifras que se consideran como medias en Bogotá. El resultado fué, en el primer caso, 4.998 gramos por litro, en el segundo 5.8 gramos por litro, y según el número que correspondía al cálculo del aparato, 8.50.

Otra causa de error consiste en que la urea no desprende todo el ázoe; para remediar esto, muchos autores emplean una pequeña cantidad de glucosa; pero haciendo el análisis por comparación con la solución de urea, el inconveniente queda subsanado.

Por otra parte, el hipobromito no obra solamente sobre la urea sino también pone en libertad el ázoe del ácido úrico, de la creatinina y de las sales amoniacales. Para eliminar el error debido al ácido úrico, se defeca previamente la orina por el subacetato de plomo; otros emplean el ácido fosfotúngstico. El error debido al amoniaco se subsana dosando el amoniaco por el procedimiento de Ronchese y relacionando la cifra urea, según la fórmula: Az $H^3 \times 0.1764$—Urea. En cuanto al error debido a la creatina, es muy pequeño para que merezca tenerse en cuenta.

Ácido úrico.—A causa de los muchos métodos que hay actualmente en boga para dosar el ácido úrico, hube de escoger varios para emplear el más preciso. El primero que emplee fué un procedimiento, también de Ronchese, que está fundado sobre la precipitación del ácido úrico al estado de urato de amoníaco, por el cloruro de amonio; este precipitado se lava con una solución de amoníaco y de cloruro de amonio y luego se disuelve a favor de un poco de ácido acético adicionado de biborato y de bicarbonato de sodio. En el líquido así preparado, se agrega poco a poco, solución

[1] A. Desgrez y J. Ayrignac, De l'influence du regime alimentaire sur la valeur des coefficients urologiques 3, R. Acad., 1906, pag. 162.

[2] A. D. Ronchese, Méthode de dosage de quelques composés azotés. Thèses de pharm., Paris, pags. 43–49.

decinormal de yodo con agua de almidón como indicador hasta la coloración azul. Cada centímetro cúbico de solución empleada equivale a 0.0084 de ácido úrico.

Este método tiene sus causas de error por la descomposición, a veces muy rápida, del yoduro de almidón, que hace que se agregue un exceso de solución de yodo.

El método del uricómetro con sulfuro de carbono como indicador, es también muy poco preciso, pues a causa de la falta de sensibilidad del indicador, se cometen errores por exceso.

Método de Folin Schoffer.—Después de la defecación de la orina por el reactivo de Folin (sulfato de amonio y acetato de uranio) se precipita el urato de amoniaco sobre 100 c. c.; el precipitado se recoge sobre un filtro, se lava y se disuelve en un medio sulfúrico donde se dosa el ácido úrico por una solución titulada de permanganato de potasio hasta la no decoloración; 1 c. c. de la solución=0.000375 de ácido úrico. Este método tiene el grave inconveniente de que la solución de permanganato se altera muy rápidamente y hay necesidad de titularla con frecuencia.

El procedimiento que elegí, por parecerme el más exacto, fué el de Garnier, que es el mismo que se emplea para las purinas y de que hablaré en seguida:

Purinas totales. Procedimiento de Hycraff Deniges Garnier.—Las bases púricas tratadas por el nitrato de plata amoniacal en presencia de una sal de magnesio dan un urato doble de plata y de magnesio perfectamente definido. Si se emplea para esta precipitación un licor de plata titulado, se puede, midiendo el exceso de plata no combinado, deducir la que se combinó en las purinas, y por consiguiente, el peso de éstas.

A 100 c. c. de orina defecada por 25 c. c. de reactivo de Folin, agréguese una solución de partes iguales de solución decinormal de nitrato de plata y de otra que contenga 350 c. c. de amoniaco, 150 gramos de cloruro de amonio y 50 gramos de cloruro de magnesio. Fíltrese, recójase 100 c. c., agréguesele 10 c. c. de una solución titulada de cianuro de potasio (equivalente a la de nitrato de plata) y 1 c. c. de solución al un décimo de yoduro de potasio. Viértase gota a gota solución decinormal de nitrato de plata hasta obtener un líquido permanentemente turbio. La solución argéntico-magnesiana da la combinación de que ya se habló, con las purinas. El cianuro de potasio se combina con el nitrato de plata que quedó libre y como son equivalentes, basta dosar con otra solución argéntica-decinormal, el cianuro que no se combinó con la plata, con KI como indicador, para saber la cantidad de la solución primitiva de nitrato de plata que se combinó con las purinas; ésta, multiplicada por 0.21 da el peso de purina por 1,000 c. c. de orina: pero a causa de la disminución de volumen que se efectuó al verificarse la defecación de la orina, hay que multiplicar este resultado por 1.25.

Como el ácido úrico es una purina, basta aislarlo, precipitándolo de la orina defecada, por el amoníaco, al estado de urato. Este precipitado se lava con sulfato de amoníaco al 10 por ciento, se disuelve por medio de una pequeña cantidad de soda al 2 por ciento en un volumen determinado de agua destilada, y en esta solución se verifica el dosado como para las purinas totales:

Bases púricas (expresadas en xantina).—Si en la precipitación de las bases púricas la relación de la plata al núcleo púrico fuera la misma que en la precipitación del ácido úrico, bastaría, para obtener la cifra de las bases púricas, restar simplemente la cifra del ácido úrico de las cifras de las purinas totales y después multiplicar esta diferencia por la relación entre el peso molecular de la purina elegida como tipo (xantina, por ejemplo) y el peso molecular del ácido úrico. Pero como en el caso de las bases cada núcleo púrico fija dos átomos de plata mientras que el núcleo del ácido úrico no fija sino uno, la misma cantidad de plata que corresponde 168 partes (una molécula) de ácido úrico, no representa sino 152:2=76 partes (media molécula) de xantina, la diferencia de las cifras experimentales multiplicada por la relación 76:168=0.454 expresa exactamente en xantina el conjunto de bases púricas.

Para obtener una expresión inequivoca delas bases púricas hay que elegir una de las dos más abundantes la adenias (151) o la xantina (152), lo que da la misma cifra,

vista la igualdad práctica de los pesos moleculares. El error proveniente de la inferioridad de los pesos moleculares de la adenina (135) y de la hipoxantina (136) debe ser compensado en gran manera por la presencia de la metilxantina (166) y de la dimetilxantina (180); se puede, pues, considerar como satisfactoria la expresión de las bases puricas en xantina.

Ázoe silicotungstico.—Por haberme sido imposible conseguir el reactivo, no pude verificar este análisis. Las materias a que él se refiere no tienen además grande importancia puesto que apenas principian a conocerse, y su importancia es, por consiguiente, muy discutible.

Fósforo urinario (en ácido fosfórico).—El método está fundado en que si se vierte una solución de una sal de uranio (nitrato o acetato), en un líquido que contenga fosfatos en medio acético, sin ácidos minerales y de una temperatura próxima a la ebullición, se obtiene un precipitado insoluble de fosfato de uranio. El fin de la reacción se conoce por medio de la tintura de cochinilla, con la cual forma la sal de uranio, cuando ya no encuentre fosfatos para combinarse, una laca verde esmeralda, o también con el ferrocianuro de potasio, que da con la sal de uranio un precipitado rojo.

Para hacer más cómoda la reacción, he titulado la solución de uranio de tal manera que 1 c. c. sea equivalente a 0.05 c. c. de ácido fosfórico por litro de orina.

La reacción se verifica en una cápsula de porcelana en la cual se pone la cantidad mencionada de orina con unas gotas de tintura de cochinilla y 1 c. c. de solución al 1 por ciento de acetato de sodio cristalizado, adicionada de 5 por ciento de acido acético cristalizable. En una bureta de Mohor que está sobre la cápsula se coloca la solución de urinario. Una vez que la orina calentada por una lámpara de alcohol, principia a desprender vapores, se deja caer, poco a poco, la solución titulada, hasta obtener el tinte verde oscuro.

Además de estos elementos, y a pesar del examen clínico, busqué en las orinas en experimento sustancias anormales para asegurarme del estado fisiológico de los individuos.

RELACIONES UROLÓGICAS.

Se sabe que los distintos elementos que encierran las orinas normales son variables con la alimentación, la edad, el sexo, el clima, etc. Por esta razón se ha dicho que no hay orinas normales absolutas sino orinas normales particulares a cada individuo.

Sin embargo, los diferentes elementos de la orina guardan entre sí relaciones que son independientes de su cantidad, y, que por ser bastante fijas, dan muchas enseñanzas respecto del funcionamiento de la nutrición.

He buscado las siguientes relaciones urológicas:

1. Relación uzoúrica: Coeficiente de oxidación (Robin) o relación de la utilización de ázoe:

$$=\frac{\text{Az U}}{\text{Az T}} \quad \frac{87 \text{ a } 90}{100} \; 0.87 \text{ a } 0.90 \text{ (según Robin).}$$

Ya se ha visto que la urea es el término final de la trasformación de las albuminoideas, de tal manera que cuanto más perfecta sea la nutrición, habrá menos intermedios y la relación Az U:Az se aproximará más a la unidad.

2. Relación del ácido fosfórico a la urea o al ázoe total $\frac{P^2\,O^5}{U}=\frac{1}{10}=\frac{10}{100}=0.10$ ó $\frac{P^2\,O^5}{Az\,T}=\frac{18}{100}=0.18$ esta relación es de una constancia notable (Ivon) cuando se eleva considerablemente se puede deducir que hay fosfaturia. Esta es relativa cuando la cifra $P^2\,O^5$ no pasa en mucho la media (2 por 60 en 24 horas), es esencial en el caso contrario. La relación $P^2\,O^5$ tiene la misma significación: $\frac{P^2\,O^5}{Az\,T}$.

3. *Relación del ácido úrico coeficiente de trasformación de las nucleoproteidas.*

Dije antes que el ácido úrico y la urea no tienen un origen común, y aunque una parte del ácido úrico es trasformado en urea en el hígado, no veo que enseñanzas prácticas pueda dar la relación entre el ácido úrico y la urea. Porque suponiendo que haya una gran trasformación de las núcleoproteidas, puede estar aumentando el ácido úrico al mismo tiempo que la urea, y entonces la relación no podrá enseñarnos nada respecto de las trasformaciones en las núcleoproteidas; o si la urea está disminuída por una débil alimentación de albuminoideos propiamente dichos y el ácido úrico aumentado por aumento de núcleoproteidos, esto no querría decir que hubiera un mal funcionamiento hepático a pesar de que la relación así lo indicara. Si hay una débil trasformación de núcleoproteidos o disminución de trasformación de las albuminoideas, el coeficiente tampoco nos enseñará nada ni respecto a un funcionamiento hepático, en el primer caso, ni respecto a una mala trasformación de núcleoproteidos, en el segundo grado. De manera que a mi modo de ver, las dos razones de ser del coeficiente indicado han perdido mucho de su importancia desde que se sabe que el ácido úrico no es un producto hacia la urea.

Yo me atrevería a proponer que se adoptara una relación entre el ázoe del ácido úrico y el ázoe de las purinas totales: $\frac{\text{Az A. U}}{\text{Az. P. T}}$; es decir, el ázoe de los núcleoproteidos que ha llegado al último grado de desintegración fisiológica, y el que ha debido llegar allí.

La investigación del ázoe de cada uno de los cuerpos que entran en el segundo factor de esta relación, complicaría demasiado las operaciones, complicación que no traería quizá mayores ventajas, una vez que se tienen cantidades de ázoe proporcionales.

Las cantidades que han servido para la relación de que hablo son, por una parte, la proporción de ázoe del ácido úrico por ciento de ázoe total y por otra parte, la de ázoe púrico total por ciento de ázoe total. Esta última cifra no representa sino el ázoe del ácido úrico más el ázoe de las purinas básicas expresadas en xantina; es decir, que en ellas no figura el ázoe aminado de la adenina y de la guanina; pero sí representan una cantidad que es siempre proporcional al ázoe púrico total propiamente dicho. Multiplicando el cociente por ciento, el resultado indicará la cantidad de ázoe púrico que para cien partes de la cifra global, llega al término normal de su desintegración fisiológica. Como se verá más adelante si en vez de tomar el tanto por ciento del ázoe total se toman las cifras directas del AU y de las BP, el resultado es muy semejante.

El coeficiente que me atrevo a proponer podría tener grande importancia para el estudio de la desintegración azoada, de las oxidaciones y desamidaciones orgánicas en general, y de la desintegración de las núcleoproteideas, en particolar; [1] tendría respecto de estas quizá la misma importancia que el coeficiente de utilización del ázoe, o mejor que el coeficiente de que hablaré en seguida, tiene respecto de las albuminoideas propiamente dichas.

4. *Imperfección urogénica—coeficiente de oxidación verdadero o de los ácidos grasos:* Si se tiene en cuenta la teoría generalmente aceptada hoy sobre la formación de la urea, se verá que es hasta cierto punto ilógico hacer intervenir el ázoe total en el coeficiente llamado "de utilización del ázoe." Considerando pues que hay cuerpos azoados que no son productos hacia la urea, Arthus [2] propuso el siguiente coeficiente:

$$\frac{\text{AZ AZUREA; AZ AMONIACAL, ÁCIDOS AMINADOS.}}{}$$

Este coeficiente fué estudiado por Maillard quien lo llamó coeficiente de imperfección urogénica y mostró su importancia como que indica además de la intensidad de la función uropoiética, el poder de oxidación del organismo sobre los ácidos grasos o cadenas carbonadas vecinas, previamente puestas en libertad.

[1] Vease página, 60. [2] M. Arthus, Précis de chimie physiologique, 1906, pág. 396; nota.

Hay que notar que para medir el amoníaco Maillar empleó el procedimiento de Ronchese, que es el mismo que he empleado yo, el cual dosa al mismo tiempo el amoníaco y los ácidos ausinados. Lazemberg insiste sobre esta necesidad de medir al mismo tiempo los ácidos aminados productores mediatos de urea, como el amoníaco [1] fué el quien le dió al coeficiente la forma notada arriba.

RESULTADOS INDIVIDUALES DE LOS ANÁLISIS.

En la primera parte de los cuadros que se verán an seguida, se encuentran los análisis hechos en Bogotá, divididos en dos series que comprenden la eliminación azoada y fosforada y luego la repartición del ázoe y la relación del fósforo al ázoe. En la primera serie se encuentran para cada cuerpo dos columnas que representan la eliminación tanto por litro, como en 24 horas.

En la segunda parte se encuentran los 20 análisis de Tunja repartidos de la misma manera, sólo que no están divididos como los Bogotá, "en clase obrera" y "clase acomodada" tanto porque su número es muy reducido como porque se refieren a individuos alimentados casi todos de la misma manera.

Por último, los análisis de cada localidad están seguidos de sus promedios y al final se encuentran los promedios generales.

CUADRO I (Serie 1ª).—*Clase obrera—Eliminación del ázoe y del fósforo.*

[Análisis de Bogotá.]

Núm.	Años de edad.	Profesión.	Densidad de la orina.	Volumen en 24 horas.	Acidez en H.		Ázoe total.	
					Por litro.	En 24 horas.	Por litro.	En 24 horas.
1	23	Jornalero	1,010	2,950	0.013	0.038	4.67	12.0
2	25	Asistente	1,022	1,460	.051	.048	6.60	9.63
3	20	Sirviente	1,018	1,850	.035	.065	8.77	16.32
4	22	Albañil	1,015	2,120	.025	.053	6.20	13.40
5	21	Sirviente	1,016	1,720	.027	.046	7.63	13.12
6	28	Carpintero	1,027	1,660	.031	.051	8.09	13.43
7	28	Jornalero	1,016	1,650	.035	.047	6.95	11.46
8	22	Gendarme	1,027	1,075	.036	.038	10.89	11.70
9	23	Latonero	1,017	2,250	.018	.040	5.35	12.00
10	25	Gendarme	1,012	1,550	.019	.029	5.10	7.90
11	25	Asistente	1,016	2,000	.024	.048	8.00	16.00
12	22	Sirviente	1,013	3,300	.005	.016	3.47	11.45
13	21	.....do	1,018	1,600	.012	.019	5.58	8.92

Núm.	Amoníaco y ácidos aminados.		Urea.		Purinas totales (en ácido úrico).		Ácido úrico.		Bases púricas (en xantina).		Ácido fosfórico.	
	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.
1	0.391	1.15	5.50	16.22	0.675	0.93	0.30	0.88	0.168	0.49	1.00	2.95
2	.408	.59	14.00	20.44	.721	1.05	.22	.32	.220	.32	1.40	2.04
3	.714	1.32	13.00	24.00	.84	1.55	.50	.92	.090	.16	1.50	2.77
4	.918	1.94	8.70	18.44	.803	1.70	.583	1.23	.099	.20	1.00	2.12
5	.969	1.66	10.00	17.20	.709	1.22	.630	1.08	.035	.06	1.20	2.06
6	.935	1.55	11.20	18.59	.966	1.60	.240	.40	.320	.52	1.60	2.66
7	.068	.11	10.94	18.05	.729	1.20	.227	.37	.220	.25	1.10	1.89
8	.561	.60	14.21	14.27	1.190	1.27	.403	.43	.350	.37	1.60	1.72
9	.204	.50	7.87	17.70	.735	1.65	.332	.14	.180	.40	.70	1.57
10	.255	.40	6.53	10.12	.735	1.14	.084	.13	.290	.45	.50	.77
11	.68	1.13	11.23	22.46	.756	1.51	.412	.82	.15	.30	1.20	2.40
12	.119	.89	7.00	23.10	.567	1.87	.229	.97	.12	.39	.60	1.98
13	.51	.82	7.52	12.00	.735	1.17	.294	.47	.20	.32	1.50	2.40

[1] Lazembérg, L'amoniaque et l'urine; étude d'un nouveau coefficient urinaire; thèse de Paris, 1912.

CUADRO II (Serie 1ª).—*Clase obrera—Eliminación del ázoe y del fósforo.*

Núm.	Años de edad.	Profesión.	Densidad de la orina.	Volumen en 24 horas (en C. c.).	Acides en H.		Ázoe total.	
					Por litro.	En 24 horas.	Por litro.	En 24 horas.
14	30	Gendarme	1,021	1,390	0.024	0.031	6.424	8.47
15	32	Cartero	1,081	920	.037	.034	14.24	13.20
16	21	Sirviente	1,018	1,980	.011	.027	6.61	13.08
17	24	Albañil	1,012	1,680	.025	.042	5.60	11.08
18	28	Carpintero	1,021	1,270	.040	.050	9.00	11.43
19	24	Asistente	1,026	1,320	.037	.048	10.416	17.92
20	24	Albañil	1,019	1,340	.031	.041	7.113	9.53
21	34	Carpintero	1,012	1,500	.020	.030	4.30	6.45
22	22	Zapatero	1,020	1,250	.048	.060	11.12	13.90
23	28	Gendarme	1,020	1,500	.012	.018	5.00	7.50
24	32	Jornalero	1,015	1,470	.012	.017	5.89	8.66
25	30	Gendarme	1,022	1,420	.011	.015	9.24	13.12
26	38	Jornalero	1,020	1,450	.050	.073	8.60	12.47

Núm.	Amoniaco y ácidos aminados.		Urea.		Purinas totales (en ácido úrico).		Ácido úrico.		Bases púricas (en xantina).		Ácido fosfóricos.	
	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.
14	0.502	0.66	9.50	12.54	0.696	0.92	0.294	0.38	0.18	0.23	1.40	1.84
15	1.275	1.17	20.20	18.58	1.365	1.25	.777	.71	.26	.23	1.00	.92
16	.442	.87	11.645	23.06	.504	.98	.336	.66	.06	.11	1.10	2.08
17	1.182	1.98	8.47	14.22	.441	.74	.252	.49	.085	.14	1.30	2.57
18	.765	.97	15.058	19.12	.840	1.06	.399	.51	.20	.25	1.30	1.64
19	1.513	1.99	24.20	31.94	.819	1.07	.525	.69	.13	.17	1.60	2.11
20	.739	.99	12.00	16.08	.693	.93	.399	.53	.132	.17	1.40	1.87
21	.204	.31	5.235	7.83	.388	.58	.20	.30	.085	.12	.50	.75
22	1.479	1.84	16.66	20.82	.714	.89	.462	.58	.113	.14	1.20	1.50
23	.194	.29	6.66	9.99	.420	.63	.231	.34	.085	.12	.70	1.05
24	.272	.39	7.293	10.72	.483	.71	.294	.43	.085	.12	1.00	1.47
25	1.275	1.82	16.82	23.88	.756	1.07	.525	.74	.104	.14	1.10	1.56
26	1.324	2.20	13.91	20.17	.462	.67	.350	.51	.050	.07	.70	1.01

CUADRO III (Serie 1ª).—*Clase obrera—Eliminación del ázoe y del fósforo.*

Núm.	Años de edad.	Profesión.	Densidad de la orina.	Volumen en 24 horas (en C. c.).	Acides en H.		Ázoe total.	
					Por litro.	En 24 horas.	Por litro.	En 24 horas.
27	24	Mózo de cordel	1,015	1,450	0.008	0.004	5.00	7.25
28	30	Carrero	1,021	1,920	.009	.017	5.10	9.69
29	28	Sastre	1,015	2,115	.019	.040	6.50	13.74
30	22	Jornalero	1,017	1,730	.009	.015	5.72	9.89
31	30	.....id	1,016	2,115	.009	.019	5.00	10.75
32	23	Herrero	1,016	2,400	.013	.031	5.92	14.20
33	35	Albañil	1,012	1,800	.021	.037	5.50	9.90
34	36	Gendarme	1,015	2,100	.015	.046	5.63	17.45
35	35	Jornalero	1,012	1,450	.027	.039	7.722	11.19
36	28	Gendarme	1,030	1,100	.016	.018	9.29	10.22
37	30	Herrero	1,015	1,470	.016	.023	8.771	12.90
38	22	Jornalero	1,016	1,700	.012	.020	3.80	6.46
39	27	Albañil	1,014	2,740	.012	.032	4.30	11.78

CUADRO III (Serie 1ª).—*Clase abrera—Eliminación del ázoe y del fosforo.—Continúa.*

Núm.	Amoniaco y ácidos aminados.		Urea.		Purinas totales (en ácido úrico).		Ácido úrico.		Bases púricas (en xantina).		Ácido fosfórico.	
	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.
27	0.90	1.30	5.70	8.26	0.399	0.57	0.105	0.15	0.132	0.19	0.60	0.87
28	1.270	2.44	6.00	11.52	.632	1.22	.221	.42	.188	.36	1.10	2.11
29	.635	1.34	9.571	20.24	.630	1.33	.200	.42	.194	.41	1.30	2.74
30	1.113	1.92	7.77	13.44	.639	1.19	.252	.43	.199	.34	1.00	1.73
31	1.270	2.73	5.00	10.75	.700	1.50	.200	.43	.230	.49	1.00	2.11
32	.399	.95	10.00	24.00	.630	1.51	.178	.42	.104	.24	1.20	2.68
33	.578	1.04	9.90	17.82	.372	.59	.210	.37	.028	.05	.60	1.08
34	.340	.95	9.219	26.58	.671	2.08	.252	.78	.190	.58	.75	2.32
35	.635	.92	10.00	14.50	.467	.68	.315	.46	.068	.09	1.60	2.32
36	.850	.93	17.20	18.92	.176	1.29	.250	.27	.418	.46	2.10	2.31
37	.476	.69	10.454	15.36	.588	.85	.378	.55	.099	.14	1.20	1.76
38	.282	.48	7.40	9.18	.756	1.29	.550	.93	.92	.15	.60	1.02
39	.300	.82	6.40	17.54	.525	1.44	.180	.49	.156	.43	.80	2.19

CUADRO IV (Serie 1ª).—*Clase obrera—Eliminación del ázoe y del fósforo.*

Núm.	Años de edad.	Profesión.	Densidad de la orina.	Volumen en 24 horas (en c. c.).	Acides en H.		Ázoe total.	
					Por litro	En 24 horas.	Por litro.	En 24 horas.
40	26	Sirviente	1,012	1,430	0.018	0.027	7.00	10.00
41	32	Jornalero	1,020	1,170	.040	.046	7.80	9.13
42	28	.....id.....	1,020	1,250	.028	.035	8.00	10.00
43	30	Carrero	1,030	1,470	.053	.078	9.57	14.07
44	20	Mozo de Cordel	1,021	1,450	.034	.049	7.20	10.40
45	20	Albañil	1,020	1,400	.025	.035	7.56	10.58
46	26	Jornalero	1,014	2,380	.015	.035	4.10	9.76
47	26	Pintor	1,021	2,150	.020	.043	7.82	16.81
48	23	Sirviente	1,022	1,370	.036	.049	10.00	13.70

Núm.	Amoniaco y ácidos aminados.		Urea.		Purinas totales (en ácido úrico).		Ácido úrico.		Bases púricas (en xantina).		Ácido fosfórico.	
	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.
40	0.221	0.32	11.00	15.73	0.839	1.20	0.450	0.54	0.175	0.25	1.50	2.14
41	.425	.50	10.00	11.70	.654	.77	.200	.23	.200	.23	2.00	2.30
42	.697	.87	6.50	8.12	.385	.48	.180	.22	.092	.11	1.20	1.50
43	1.250	1.84	11.95	17.57	.735	1.08	.400	.59	.151	.22	1.00	1.47
44	.700	1.01	13.40	19.43	.420	.61	.170	.25	.113	16	2.00	2.90
45	.969	1.36	9.17	12.84	.567	.79	.214	.30	.159	.22	1.00	1.40
46	.255	.61	5.00	11.90	.523	1.24	.180	43	.155	.36	.90	2.14
47	1.105	2.37	10.00	21.50	.751	1.61	.201	.42	.249	.53	1.20	2.58
48	1.168	1.60	10.10	17.94	.799	1.08	.356	.49	.109	.15	2.00	2.74

CUADRO V (Serie 1ª).—*Clase acomodada—Eliminación del ázoe y del fósforo.*

Núm.	Años de edad.	Profesión.	Densidad de la orina.	Volumen en 24 horas (en c. c.).	Acidez en H.		Ázoe total.	
					Por litro.	En 24 horas.	Por litro.	En 24 horas.
1	20	Estudiante	1,022	1,660	0.032	0.053	5.00	8.30
2	22	Comerciante	1,018	1,400	.046	.062	9.223	12.91
3	24	Estudiante	1,016	2,680	.020	.054	5.25	14.07
4	24	.....id	1,020	3,100	.012	.037	4.00	12.40
5	25	.....id	1,021	1,300	.055	.071	10.00	13.00
6	27	Médico	1,030	1,600	.027	.043	7.10	11.36
7	26	Estudiante	1,020	1,000	.047	.047	16.21	16.21
8	27	Médico	1,020	1,800	.034	.061	11.00	19.80
9	25	Estudiante	1,021	1,880	.027	.053	6.75	12.69
10	26	.....id	1,021	1,320	.044	.058	9.50	12.54
11	26	.....id	1,020	1,800	.033	.051	11.60	20.88
12	25	Médico	1,022	2,000	.012	.024	6.20	12.40
13	24	Estudiante	1,022	1,360	.026	.035	5.648	7.68
14	24	Militar	1,021	1,230	.023	.027	9.58	11.78

Núm.	Amoniaco y ácidos aminados.		Urea.		Purinas totales (en ácido úrico).		Acido úrico.		Bases púricas (en xantina).		Ácido osfórico.	
	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.
1	0.60	1.00	8.10	13.45	0.801	1.33	0.262	0.43	0.244	0.40	1.30	2.16
2	.689	.95	11.90	16.06	.727	1.02	.332	.46	.178	.25	1.50	2.10
3	.521	1.39	8.72	23.40	.302	.81	.148	.40	.069	.18	1.00	2.68
4	.541	1.68	5.90	18.29	.588	1.26	.300	.96	.190	.40	.80	2.48
5	1.290	1.67	13.00	16.90	.829	1.08	.501	.65	.148	.19	.96	1.25
6	.646	1.03	12.00	19.20	1.076	1.72	.350	.53	.328	.52	1.00	1.60
7	1.211	1.21	25.00	25.00	1.0825	1.08	1.555	.55	.240	.24	2.40	2.40
8	.888	1.59	16.00	28.80	.850	1.53	.243	.44	.274	.49	.75	1.35
9	.544	1.02	12.00	21.56	.964	1.81	.301	.56	.300	.56	.60	1.13
10	.612	.81	16.10	21.25	.7575	1.07	.180	.24	.261	.34	1.06	1.40
11	.816	1.47	18.00	32.20	.540	.97	.168	.30	.168	.30	1.60	2.88
12	.225	.45	7.20	14.40	.840	1.68	.261	.52	.282	.56	1.80	1.60
13	.558	.75	7.18	9.76	.903	1.23	.420	.57	.118	.16	1.00	1.36
14	.357	.44	16.40	20.17	1.023	1.26	.742	.91	.125	.15	1.80	2.21

CUADRO VI (Serie 1ª).—*Clase acomodada—Eliminación del ázoe y del fósforo.*

Núm.	Años de edad.	Profesión.	Densidad de la orina.	Volumen en 24 horas (en c.c.).	Acidez en H.		Ázoe total.	
					Por litro.	En 24 horas.	Por litro.	En 24 horas.
15	23	Químico	1,030	1,300	0.051	0.063	13.23	17.20
16	24	Estudiante	1,021	1,340	.027	.036	5.27	7.06
17	34	Hacendado	1,022	1,800	.020	.036	10.70	19.26
18	25	Estudiante	1,030	980	.055	.053	6.00	15.68
19	23	.....id	1,025	1,250	.037	.072	11.30	14.12
20	24	.....id	1,017	1,500	.015	.022	9.53	14.29
21	25	.....id	1,014	1,580	.024	.038	10.84	16.48
22	25	Militar	1,014	2,740	.012	.033	4.35	2.52
23	33	Estudiante	1,032	850	.040	.034	13.82	11.88
24	36	.....id	1,031	1,000	.035	.035	8.10	8.10
25	28	Comerciante	1,020	1,450	.006	.009	10.00	14.50
26	27	Médico	1,020	1,550	.059	.091	10.00	15.50
27	26	Estudiante	1,024	1,250	.022	.027	10.861	13.58
28	25	.....id	1,014	1,760	.005	.009	9.35	16.46

CUADRO VI (Serie 1ª).—*Clase acomodada—Eliminación del ázoe y del fósforo*—Con.

Núm.	Amoníaco y ácidos aminados.		Urea.		Purinas totales (en ácido úrico).		Ácido úrico.		Bases púricas (en xantina).		Ácido fosfórico.	
	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.
15	1.279	1.66	20.60	26.78	1.050	1.36	0.503	0.65	0.247	0.32	1.80	2.34
16	.595	.80	8.70	11.66	.693	.93	.273	.36	.190	.25	.90	1.21
17	.510	.92	17.72	31.90	.553	.99	.231	.41	.145	.27	2.00	3.60
18	1.193	1.17	25.887	25.37	1.701	1.67	.609	.60	.492	.48	1.90	1.86
19	.996	1.23	20.66	25.83	1.050	1.31	.315	.39	.326	.40	2.10	2.26
20	1.00	1.50	14.73	22.15	.945	1.42	.470	.70	.215	.32	1.30	1.95
21	.949	1.50	14.72	23.26	.399	.61	.150	.24	.12	.18	1.50	2.40
22	.440	1.20	7.40	20.27	.425	1.15	.160	.38	.119	.33	.70	1.92
23	1.453	1.25	19.60	16.86	.632	.54	.491	.42	.064	.05	2.10	1.80
24	1.031	1.03	12.22	12.22	1.356	1.36	.636	.64	.325	.32	1.00	1.00
25	.551	.80	15.686	20.74	.462	.67	.211	.30	.113	.16	1.30	1.88
26	.754	1.17	16.49	24.01	.462	.72	.357	.55	.047	.07	1.00	1.55
27	1.072	1.34	19.296	24.12	.681	.85	.508	.63	.078	.10	2.10	2.62
28	.732	1.29	15.00	26.40	.509	.80	.383	.67	.057	.10	1.20	2.11

ELIMINACIÓN DEL ÁZOE Y DEL FÓSFORO—ANÁLISIS DE TUNJA.

Núm.	Años de edad.	Profesión.	Densidad de la orina.	Volumen en 24 horas.	Acidez en H.		Ázoe total.	
					Por litro.	En 24 horas.	Por litro.	En 24 horas.
1	30	Abogado	1,019	1,340	0.031	0.041	9.23	12.35
2	44	.....Id	1,016	1,700	.012	.020	3.80	6.46
3	29	Comerciante	1,016	2,060	.021	.043	7.32	15.07
4	42	Ingeniero	1,018	2,090	.012	.025	4.83	10.09
5	29	Medico	1,021	1,230	.023	.027	9.58	11.78
6	38	Sacerdote	1,017	1,930	.028	.054	8.20	14.12
7	20	Sirviente	1,012	2,600	.010	.026	3.60	9.36
8	45	Institutor	1,015	2,000	.024	.048	4.50	9.00
9	24	Soldado	1,015	2,900	.027	.078	4.13	11.98
10	22	.....id	1,010	2,800	.013	.036	2.06	5.77

Núm.	Amoníaco y ácidos aminados.		Urea.		Purinas totales (en ácido úrico).		Ácido úrico.		Bases puricas (en xantina).		Ácido fosfórico.	
	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.
1	0.74	0.99	12.00	16.08	0.70	0.93	0.40	0.53	0.132	0.17	1.40	1.87
2	.28	.48	7.40	9.18	.76	1.29	.55	.93	.090	.14	1.20	1.76
3	.51	1.05	12.90	26.57	.46	.95	.35	.73	.051	.10	1.08	2.22
4	.36	.75	7.90	16.52	.29	.61	.24	.50	.020	.05	.64	1.33
5	.36	.44	16.40	20.17	1.02	1.26	.74	.91	.013	.15	1.80	2.21
6	.52	1.09	11.30	21.81	.52	1.09	.32	.42	.091	.17	1.10	2.02
7	.40	1.04	5.80	15.08	.34	.88	.18	.47	.070	.18	.60	1.56
8	.68	1.36	5.10	10.20	.76	1.52	.41	.82	.151	.30	.60	1.20
9	.24	.70	4.86	13.93	.44	1.27	.31	.90	.059	.17	.90	2.61
10	.20	.56	3.43	9.60	.41	1.16	.23	.64	.081	.18	.60	1.68

ANÁLISIS DE TUNJA—ELIMINACIÓN DEL ÁZOE Y DEL FÓSFORO.

Núm.	Años de edad.	Profesión.	Densidad de la orina.	Volumen en 24 horas.	Acides en H.		Ázoe total.	
					Por litro.	En 24 horas.	Por litro.	En 24 horas.
11	21	Soldado.....	1,016	2,450	0.022	0.054	2.94	7.20
12	21	.....id.....	1,012	3,300	.021	.059	3.33	10.99
13	22	.....id.....	1,014	3,150	.021	.066	3.80	11.97
14	22	.....id.....	1,015	2,950	.023	.068	4.10	12.09
15	24	.....id.....	1,008	3,100	.018	.055	3.81	11.81
16	22	.....id.....	1,010	3,240	.021	.068	2.86	9.26
17	21	.....id.....	1,014	3,020	.022	.066	4.44	13.51
18	21	.....id.....	1,011	2,900	.026	.065	4.84	14.04
19	22	.....id.....	1,014	3,200	.021	.067	4.20	13.44
20	22	.....id.....	1,012	3,000	.024	.072	4.60	13.80

Núm.	Amoniaco y ácidos-aminados.		Urea.		Purinas totales (en ácido úrico).		Ácido úrico.		Bases puricas (en xantina).		Ácido fosfóricos.	
	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.
11	0.20	0.49	4.86	11.81	0.55	1.59	0.32	0.78	0.104	0.255	0.60	1.47
12	.27	.89	4.77	15.54	.45	1.48	.11	.36	.154	.508	.45	1.49
13	.23	.72	5.10	16.07	.46	1.45	.20	.63	.114	.359	.50	1.58
14	.20	.59	4.90	14.46	.42	1.24	.18	.53	.109	.322	.80	2.36
15	.21	.65	5.71	16.03	.42	1.30	.28	.87	.063	.195	.70	2.17
16	.31	1.00	3.43	11.11	.45	1.45	.19	.62	.118	.382	.60	1.94
17	.44	1.33	5.14	15.42	.22	.66	.11	.33	.048	.145	.40	1.20
18	.53	1.58	5.57	16.15	.46	1.33	.26	.75	.091	.201	.40	1.20
19	.48	1.53	4.80	15.36	.48	1.53	.18	.58	.091	.291	.80	2.56
20	.24	.72	5.00	15.00	.44	1.32	.15	.45	.132	.396	.90	2.70

Los cuadros de la segunda serie están también divididos en tres partes y cada uno de los números corresponde a los mismos individuos que figuran en los cuadros anteriores. En los cuadros, que se verán en seguida, se encuentra la repartición del ázoe, según los distintos materiales eliminados en 24 horas.

El cálculo del ázoe, que corresponde a cada uno de los materiales, fué hecho de la manera siguiente:

Para obtener el ázoe amoniacal basta multiplicar el amoniaco por $\frac{Az}{AzH^3}=\frac{14}{17}=0.824$.

El ázoe de la urea se obtiene multiplicando por la urea a $\frac{Az^2}{CO\overline{Az^2H^4}}=\frac{28}{60}=0.4667$. El ázoe de la xantina, multiplicando a esta por $\frac{Az^4}{C^5H^4\overline{Az^4O^2}}=\frac{56}{152}=0.3648$. El ázoe del ácido úrico es igual a $\frac{Az^4}{C^5H^4\overline{Az^4O^3}}=\frac{56}{168}=0.334=1/3$, de modo que para obtener el ázoe del ácido úrico basta multiplicar la cifra obtenida de este ácido en las 24 horas por .334, o sacarle la tercera parte.

El ázoe púrico total es la suma de los dos anteriores. Representa, como ya dije, el núcleo púrico solamente, y no comprende el ázoe aminado de la adenina y de la guanina.

En estos mismos cuadros se encuentra también el tanto por ciento del ázoe con que cada uno de estos cuerpos contribuye a la cifra del ázoe total.

La suma de éstos tantos por ciento representa la cantidad de ázoe determinado, por oposición lo que se llama en el cuadro fracción de ázoe indeterminado; es decir, de todas las sustancias que no han sido dosadas individualmente.

En las últimas líneas de los cuadros se encontrará el fósforo de los fostatos el cual se obtiene multiplicando la cifra de P^2O^5 por $\frac{P^2}{P^2O^5}=\frac{62}{162}=0.437$.

Hecho esto basta dividir la cifra del ázoe total por la del fósforo para obtener la relación ponderal del ázoe al fósforo $\frac{Az}{P}$. Multiplicando esta relación ponderal por la relación inversa de los pesos atómicos $\frac{31}{14}=2.214$ se obtiene el número de átomos de ázoe que corresponde a un átomo de fósforo.

Esta relación atómica del ázoe al fósforo es interesante, porque el denominador indica el número de átomos de ázoe que deja el organismo mientras se elimina un átomo de fósforo. Esta representación sería perfecta si se hubiera dosado al mismo tiempo que el fósforo de los fosfatos, todo el que pueda acompañarle en formas diferentes. Se sabe, sin embargo, que esta excreción del fósforo es muy pequeña; de manera que si la relación $\frac{P}{Az}$ del cuadro no es de una rigurosa exactitud, sí se acerca mucho a la realidad.

CUADRO I–II (Serie 2ª).—*Clase obrera—Repartición del ázoe y relación del fósforo al ázoe.*

Números.	1	2	3	4	5	6	7	8	9	10
Ázoe amoniacal	0.95	0.49	1.05	1.60	1.39	1.30	0.10	0.49	0.41	0.33
Ázoe de la urea	7.58	9.54	11.20	8.61	8.08	8.68	8.42	6.66	8.26	4.71
Ázoe del ácido úrico	.294	.106	.306	.411	.361	.134	.123	.144	.247	.043
Ázoe de las bases púricas	.180	.118	.059	.073	.022	.191	.092	.136	.147	.166
Ázoe púrico total	.474	.224	.365	.484	.383	.325	.255	.280	.394	.209
Ázoe total	12.00	9.63	16.32	13.40	13.12	13.43	11.46	11.70	12.00	7.90
Parte del ázoe amoniacal por 100 de ázoe total	7.92	5.08	6.43	11.94	10.52	9.68	1.15	4.19	3.42	4.18
Parte del ázoe de la urea por 100 de ázoe total	63.17	83.25	62.50	64.25	61.10	64.62	73.47	56.92	68.83	59.62
Parte del ázoe de las bases púricas por 100 de ázoe total	1.50	1.22	.36	.54	.17	1.42	.80	1.16	1.22	2.10
Parte del ázoe del ácido úrico por 100 de ázoe total	2.45	1.10	1.87	307.00	2.75	1.00	107.00	1.23	2.06	.54
Parte ázoe púrico total por 100 de ázoe total	3.95	2.33	2.23	3.61	2.92	2.42	1.87	1.39	3.28	2.64
Fracción de ázoe determinado por 100	75.04	90.65	71.16	79.80	74.54	76.72	76.43	62.50	75.53	66.44
Fracción de ázoe indeterminado por 100	24.96	9.35	28.84	20.20	25.46	23.28	23.57	37.50	24.47	33.56
Anhídrido fosfórico	9.95	2.04	2.77	2.12	2.06	2.66	1.89	1.72	1.57	.77
Fósforo de los fosfatos	1.29	.89	1.21	.93	..90	1.16	.82	.75	.69	.34
Relación ponderal	9.30	10.82	13.49	14.41	14.58	11.58	13.97	15.60	17.39	23.23
Relación atómica	20.60	23.90	29.90	31.90	32.30	25.60	30.90	34.50	38.50	51.40

Números.	11	12	13	14	15	16	17	18	19	20
Ázoe amoniacal	0.92	0.32	0.67	0.54	0.96	0.72	1.63	0.80	1.64	0.81
Ázoe de la urea	10.48	10.78	5.70	5.88	8.67	10.76	6.64	8.92	14.91	7.50
Ázoe del ácido úrico	.273	.322	.157	.127	.237	.220	.164	.170	.230	.177
Ázoe de las bases púricas	.110	.143	.118	.085	.085	.040	.051	.092	.062	.062
Ázoe púrico total	.383	.465	.275	.212	.322	.260	.215	.262	.292	.239
Ázoe total	16.00	11.45	8.92	8.47	13.26	13.20	11.08	11.43	17.92	9.43
Parte del ázoe amoniacal por 100 de ázoe total	5.75	7.79	7.54	6.37	7.27	5.50	14.75	6.98	9.15	8.50
Parte del ázoe de la urea por 100 de ázoe total	65.37	73.77	62.78	69.08	65.83	82.26	59.93	78.04	83.20	78.70
Parte del ázoe del ácido úrico por 100 de ázoe total	1.71	2.81	1.76	1.50	1.79	1.68	1.48	1.49	1.29	1.75
Parte de ázoe de las bases púricas por 100 de ázoe total	.60	1.25	1.33	1.00	.64	.31	.46	.81	.34	.66
Parte ázoe púrico total por 100 ázoe total	2.40	4.06	3.09	2.50	2.43	1.99	1.94	2.30	1.63	2.41
Fracción de ázoe determinado por 100	73.52	85.62	73.31	77.96	75.53	89.75	76.58	87.32	93.98	89.61
Fracción de ázoe indeterminado por 100	26.48	14.38	26.69	22.05	24.47	10.25	23.42	12.68	6.02	10.39
Anhídrido fosfórico	2.40	1.98	2.40	1.84	.92	2.08	2.57	1.64	2.11	1.87
Fósforo de los fosfatos	1.05	.86	1.05	.80	.40	.91	1.12	.72	.92	.82
Relación ponderal	15.24	13.31	8.49	10.59	33.00	14.37	9.89	17.26	18.39	11.62
Relación atómica	33.70	29.50	18.80	23.40	73.00	31.70	21.90	38.20	40.70	25.70

CUADRO III-IV (Serie 2ª).—*Clase obrera—Repartición del ázoe y relación del fósforo al ázoe.*

Números.	21	22	23	24	25	26	27	28	29	30
Ázoe amoniacal	0.25	1.52	0.24	0.32	1.50	1.81	1.07	2.01	1.11	1.58
Ázoe de la urea	3.63	9.72	4.66	5.00	11.14	9.41	3.85	5.38	9.44	6.27
Ázoe del ácido úrico	.100	.193	.113	.143	.247	.170	.050	.140	.140	.143
Ázoe de las bases púricas	.044	.051	.044	.044	.051	.025	.070	.132	.151	.125
Ázoe púrico total	.144	.244	.157	.187	.298	.195	.120	.272	.291	.268
Ázoe total	6.45	13.90	7.50	8.66	13.12	2.47	7.25	9.69	13.74	9.89
Parte del ázoe amoniacal por 100 de ázoe total	3.47	11.63	3.19	3.70	11.42	14.53	14.77	20.74	8.06	15.99
Parte del ázoe de la urea por 100 de ázoe total	56.28	69.92	62.13	57.73	83.99	75.46	53.10	55.52	68.70	63.40
Parte del ázoe del ácido úrico por 100 de ázoe total	1.55	1.39	1.51	1.65	1.88	1.36	.69	1.44	1.19	1.44
Parte del ázoe de las bases púricas por 100 de ázoe total	.68	.37	.59	.51	.39	.20	.99	1.34	1.10	1.25
Parte ázoe púrico total por 100 ázoe total	2.23	1.76	2.10	2.16	2.27	1.56	1.68	2.78	2.29	2.69
Fracción de ázoe determinado por 100	61.98	83.31	67.42	63.59	97.68	91.55	69.55	79.04	79.05	82.08
Fracción de ázoe indeterminado por 100	38.02	16.69	32.58	36.41	2.32	8.45	30.45	20.96	20.95	17.92
Anhídrido fosfórico	.75	1.50	1.05	1.47	1.56	1.01	.87	2.11	2.74	1.08
Fósforo de los fosfatos	.33	.65	.46	.64	.68	.44	.38	.92	1.20	.47
Relación ponderal	19.54	21.38	16.30	13.53	19.22	28.34	18.95	10.53	11.45	21.04
Relación atómica	43.30	47.30	36.00	29.90	42.50	62.70	41.90	23.30	25.30	46.60

Numeros.	31	32	33	34	35	36	37	38	39	40
Ázoe amoniacal	2.25	0.13	0.86	.078	0.76	0.77	0.58	0.39	0.67	0.26
Ázoe de la urea	5.02	11.20	8.32	13.34	6.77	8.33	7.17	4.28	8.18	7.34
Ázoe del ácido úrico	.144	.140	.123	.260	.154	.090	.195	.311	.164	.180
Ázoe de las bases púricas	.180	.068	.018	.215	.033	.169	.051	.055	.158	.092
Ázoe púrico total	.324	.222	.141	.475	.187	.259	.246	.366	.322	.272
Ázoe total	10.75	14.20	9.90	17.45	11.19	11.22	12.90	6.46	11.78	10.
Parte del ázoe amoniacal por 100 de ázoe total	20.93	5.49	8.69	4.47	6.79	6.86	4.50	6.04	5.68	2.60
Parte del ázoe de la urea por 100 de ázoe total	46.70	78.87	84.04	76.45	60.50	78.68	55.58	66.25	69.44	74.40
Parte del ázoe del ácido úrico por 100 de ázoe total	1.34	.98	1.24	1.49	1.38	.80	1.51	4.83	1.39	1.80
Parte del ázoe de las bases púricas por 100 de ázoe total	1.67	.62	.19	1.29	.29	1.51	.40	.85	1.34	.92
Parte ázoe purico total por parte ázoe purico total por 100 ázoe total	3.01	1.60	1.43	2.78	1.67	2.31	1.91	5.68	2.73	2.72
Fracción de ázoe determinado por 100	69.30	85.96	94.16	83.70	68.96	87.85	71.99	76.97	77.85	98.72
Fracción de ázoe indeterminado por 100	30.70	14.04	5.84	16.30	31.04	12.15	28.01	23.03	22.15	21.28
Anhidrido fosforico	2.11	2.68	1.08	2.32	2.32	2.31	1.76	1.02	2.19	2.14
Fósforo de los fosfatos	.92	1.17	.47	1.01	1.01	1	.77	.44	.96	.93
Relación ponderal	11.47	12.14	21.06	17.23	11.08	11.22	19.27	14.40	11.12	10.75
Relación atómica	25.4	26.9	46.6	38.1	24.5	24.8	42.7	32.5	24.6	23.8

CUADRO V-VIII (Serie 2ª).—*Clase acomodada—Repartición del ázoe y relación del fósforo al ázoe.*

Números.	41	42	43	44	45	46	47	48
Ázoe amoniacal	0.11	0.71	1.52	0.83	1.12	0.51	1.95	1.32
Ázoe de la urea	5.46	3.79	8.20	9.07	5.99	5.55	11.71	8.37
Ázoe del ácido úrico	1.076	.073	.197	.083	.100	.143	.140	.163
Ázoe de las bases púricas	.084	.040	.081	.059	.081	.133	.195	.055
Ázoe púrico total	.150	.113	.278	.142	.181	.276	.335	.218
Ázoe total	9.13	10	14.07	10.40	10.58	9.76	16.81	12.70
Parte del ázoe amoniacal por 100 de ázoe total	4.47	7.10	10.80	7.98	10.54	5.02	11.60	9.93
Parte del ázoe de la urea por 100 de ázoe total	59.80	37.90	58.23	87.21	56.62	56.86	69.66	61.09
Parte del ázoe de ácido úrico por 100 de ázoe total	.83	.78	1.40	.80	.95	1.47	.83	1.19
Parte del ázoe de las bases púricas por 100 de ázoe total	.90	.40	.57	.57	.76	1.36	1.16	.40
Parte ázoe purico total por 100 ázoe total	1.73	1.13	1.97	1.45	1.71	2.83	1.99	1.59
Fracción de ázoe determinado por 100	66	46.13	71.05	96.64	68.92	64.71	83.25	72.31
Fracción de ázoe indeterminado por 100	44	53.87	28.95	3.36	31.08	35.29	16.75	27.69
Anhidrido fosfórico	1	.65	.64	1.27	.61	.93	1.13	1.20
Relación ponderal	9.13	15.38	21.96	8.19	17.34	10.49	14.88	1.42
Relación atómica	20.2	34	48.7	81.1	38.4	23.2	32.9	31.4

CUADRO V-VIII (Serie 2ª).—*Clase acomodada—Repartición del ázoe y relación del fósforo al ázoe*—Continúa.

Números.	1	2	3	4	5	6	7	8	9	10
Ázoe amoniacal	0.82	0.79	1.14	1.38	1.38	0 85	1	1.21	0 84	0.67
Ázoe de la urea	6.38	8.43	10.52	8.54	7.89	8.96	11.67	13.44	10.06	9.92
Ázoe del ácido úrico	.144	.154	.134	.321	.277	.177	.184	.147	.197	.080
Ázoe de las bases púricas	.147	.092	.066	.147	.070	.191	.088	.180	.206	.125
Ázoe púrico total	.291	.246	.200	.468	.347	.368	.272	.327	.393	.205
Ázoe total	8.30	12.91	14.07	12.40	13	11.36	16.21	19.80	12.69	12.54
Parte del ázoe amoniacal por 100 de ázoe total	9.88	6.12	8.10	11.13	10.61	7.48	6.17	6.62	6.62	5.34
Parte del ázoe de la urea por 100 del ázoe total	76.87	65.22	74.77	68.87	60.19	78.88	71.99	67.88	79.27	79.11
Parte del ázoe del ácido úrico por 100 de ázoe total	1.77	.80	.47	1.10	.54	1.68	.54	.91	1.62	1
Parte ázoe púrico total por 100 del ázoe total	90.25	73.33	84.31	83.36	73.59	89.60	79.83	76.15	88.98	86.07
Parte ázoe púrico indeterminado por 100 de ázoe total	9.75	26.67	15.69	16.64	26.41	10.40	20.17	23.85	11.02	13.93
Anhidrido fosfórico	2.16	2.10	2.68	2.48	1.25	1.60	2.40	1.35	1.13	1.40
Fósforo de los fosfatos	.95	.92	1.17	1.08	1.54	1.70	1.05	.59	.49	.61
Relación ponderal	8.59	14.06	12.01	11.44	23.85	16.25	15.45	33.56	25.90	20.52
Relación atómica	29	31.1	26.1	25.5	52.8	36	34.3	74.3	57.3	45.4

Números.	11	12	13	14	15	16	17	18	19	20
Ázoe amoniacal	1.21	0.79	0.63	0.36	1.37	0.66	0.76	0.96	0.91	1.24
Ázoe de la urea	15.03	6.72	4.55	9.41	12.50	5.44	14.89	11.84	12.05	10.33
Ázoe del ácido úrico	.100	.174	.190	.304	.217	.120	.137	.200	.130	.284
Ázoe de las bases púricas	.110	.206	.059	.055	.108	.092	.099	.177	.147	.177
Ázoe púrico total	20.80	12.40	7.68	11.78	17.20	7.06	19.26	15.68	14.12	14.29
Parte del azoe amoniacal por 100 de ázoe total	5.72	6.21	8.22	3.06	7.96	9.35	3.95	6.12	6.44	8.68
Parte del ázoe de la urea por 100 de ázoe total	72.45	54.19	59.24	79.88	72.74	76.49	77.31	75.45	85.34	72.21
Parte del ázoe de ácido úrico por 100 de ázoe total	4.79	1.40	2.45	2.58	1.26	1.69	.71	1.27	.92	1.64
Parte del ázoe de las bases púricas por 100 ázoe total	5.26	1.66	.77	.47	.63	1.30	.51	1.29	1.04	.81
Parte ázoe purico total por 100 de ázoe total	10.05	3.06	3.22	3.05	1.89	2.99	1.22	2.56	1.96	2.45
Fracción de ázoe determinado por 100	88.22	63.46	70.68	85.99	82.59	88.83	82.58	84.13	93.74	83.34
Fracción de ázoe indeterminado por 100	11.78	36.54	29.32	14.01	17.41	11.17	17.42	15.87	6.26	16.66
Anhidrido fosfórico	2.88	1.60	1.36	2.21	2.34	1.21	3.60	1.86	2.26	1.95
Fósforo de los fosfatos	1.25	.70	.59	.96	1.02	.53	1.57	.81	.99	.85
Relación ponderal	16.70	17.71	13	12.37	16.86	13.21	12.27	19.26	14.28	16.81
Relación atómica	37	39.2	28.8	27.4	37.3	29.2	27.2	42.6	31.6	37.2

Números.	21	22	23	24	25	26	27	28
Ázoe amoniacal	1.24	0.99	1.03	0.85	0.66	0.96	0.10	1.06
Ázoe de la urea	10.85	9.46	7.86	5.70	9.68	11.20	11.27	12.32
Ázoe del ácido úrico	.080	.127	.140	.214	.100	.195	.210	.224
Ázoe de las bases púricas	.066	.121	.018	.117	.059	.026	.037	.037
Ázoe púrico total	.146	.248	.158	.331	.159	.221	.247	.261
Ázoe total	16.48	12.52	11.88	8.10	14.50	15.50	13.58	16.46
Parte del ázoe amoniacal por 100 de ázoe total	7.52	7.91	8.67	10.49	4.55	6.19	8.10	6.44
Parte del ázoe de la urea por 100 de ázoe total	65.84	75.56	66.17	70.37	66.76	72.26	82.90	74.85
Parte del ázoe del ácido úrico por 100 de ázoe	1.47	1.01	1.18	2.64	.69	1.25	1.54	1.36
Parte del ázoe de las bases púricas por 100 de ázoe total	.40	.97	.15	1.44	.41	.17	.27	.22
Parte ázoe purico total por 100 ázoe total	.87	1.98	1.33	4.08	1.10	1.42	1.81	1.58
Fracción de ázoe determinado por 100	74.23	85.45	23.83	15.06	27.59	20.13	7.19	17.13
Anhidrido fosfórico	2.40	1.92	1.80	1	1.88	1.55	2.62	2.11
Fósforo de los fosfatos	1.05	.84	.78	.44	.82	.68	1.14	.92
Relación ponderal	15.69	14.67	15.23	18.41	17.68	22.79	11.91	16.80
Relación atómica	34.7	32.5	33.7	40.8	39.1	50.4	26.4	37.2

CUADRO I–II (Serie 2).—*Repartición del ázoe ó relación del fósforo al ázoe.*

[Análisis hechos en Tunja.]

Números.	1	2	3	4	5	6	7	8	9	10
Ázoe amoniacal	0.81	0.89	0.87	0.62	0.36	0.30	0.86	0.93	0.58	0.46
Ázoe de la urea	7.50	4.28	12.40	7.71	9.41	10.18	7.04	4.75	6.41	3.31
Ázoe del ácido úrico	.18	.31	.243	.167	.304	.14	.16	.27	.30	.21
Ázoe de las bases púricas	.062	.060	.037	.018	.055	.062	.070	.110	.060	.061
Ázoe púrico total	.242	.37	.280	.185	.359	.202	.23	.38	.36	.86
Ázoe total	12.35	6.46	15.07	10.09	11.78	14.12	9.36	9.00	11.95	5.77
Parte del ázoe amoniacal por 100 de ázoe total	6.56	6.04	5.77	6.14	3.06	2.12	11.32	10.33	14.85	7.80
Parte del ázoe de la urea por 100 de ázoe total	60.73	66.25	82.28	76.41	79.88	72.10	75.21	52.74	52.89	57.37
Parte del ázoe del ácido úrico por 100 del ázoe total	1.46	4.83	1.59	1.68	2.58	.98	1.70	3.00	2.61	3.64
Parte del ázoe de las bases púricas por 100 de ázoe total	.50	.85	.25	.18	.47	.44	.75	1.22	.52	1.12
Parte del ázoe púrico total por 100 de ázoe total	1.96	5.68	1.84	1.86	3.05	1.42	2.45	4.22	3.13	4.76
Fracción del ázoe determinado por 100	77.75	76.97	89.89	86.27	85.99	76.64	88.98	67.29	60.87	69.93
Fracción del ázoe indeterminado por 100	22.25	23.03	10.10	13.73	14.01	23.36	11.02	32.71	39.13	30.07
Anhidro fosfórico	1.87	1.02	2.22	1.33	2.21	2.12	1.56	1.20	2.61	1.49
Fósforo de los fosfatos	.82	.44	.97	.58	.96	.93	.69	.52	.93	.65
Relación ponderal	14.96	14.40	15.55	17.33	12.37	14.10	15.30	17.30	12.85	8.88
Relación atómica	11.1	32.5	34.4	38.5	27.4	51.2	33.9	38.2	28.4	12.3

Números.	11	12	13	14	15	16	17	18	19	20
Ázoe amoniacal	0.39	0.73	0.59	0.49	0.54	0.82	1.09	1.38	1.26	0.59
Ázoe de la urea	5.92	7.26	7.51	6.75	7.49	5.19	7.19	7.54	7.17	7.00
Ázoe del ácido úrico	.23	.12	.21	.18	.26	.20	.11	.25	.19	.15
Ázoe de las bases púricas	.93	.185	.131	.118	.070	.134	.053	.072	.106	.263
Ázoe púrico total	.323	.305	.341	.298	.330	.339	.163	.322	.296	.413
Ázoe total	7.20	10.99	11.97	12.09	11.81	9.26	13.46	14.04	13.44	13.80
Parte del ázoe amoniacal por 100 de ázoe total	5.36	6.64	4.97	4.05	4.57	8.96	8.13	9.83	9.37	4.23
Parte del ázoe de la urea por 100 del ázoe total	82.22	66.05	65.26	55.00	63.42	56.72	53.73	53.53	53.34	51.23
Parte del ázoe del ácido úrico por 100 de ázoe total	4.55	1.09	1.75	1.49	2.20	2.21	.82	1.85	1.41	1.09
Parte del ázoe de las bases púricas por 100 de ázoe total	1.29	1.68	1.18	.98	.593	1.508	.395	.513	.79	1.18
Parte del ázoe púrico total por 100 de ázoe total	5.84	2.77	1.93	2.47	.793	3.718	1.215	2.363	2.20	2.27
Fracción del ázoe determinado por 100	93.42	75.46	73.15	60.52	70.78	69.39	74.07	65.72	64.91	57.73
Fracción del ázoe indeterminado por 100	6.58	24.54	26.84	39.48	29.22	30.61	25.93	34.28	35.09	42.27
Anhidro fosfórico	1.47	1.49	1.58	2.36	2.17	1.94	1.20	1.20	2.56	2.70
Fósforo de los fosfatos	.64	.65	.69	.63	.94	.85	.52	.52	1.12	1.18
Relación ponderal	11.25	16.91	17.35	11.72	12.56	10.76	25.77	27.38	12.00	11.69
Relación atómica	24.09	27.04	35.3	25.9	27.8	23.8	57.00	60.6	26.6	25.9

Promedios de Bogotá.

	Clase obrera.	Clase acomodada.	Promedios generales.
Densidad	1.018	1.021	1.019
Volumen en 24	1.727	1.590	1.658
Ácidez (en H)	.037	.044	.040
Ázoe total	11.29	13.59	12.44
Amoníaco y ácidos aminados	1.37	1.15	1.26
Urea	16.84	21.21	19.02
Purinas totales (en ácido úrico)	1.12	1.12	1.12
Ácido úrico	.52	.52	.52
Bases púricas (en xantina)	.26	.25	.25
Ázoe amoniacal	1.13	.95	1.04
Ázoe de la urea	7.86	9.90	8.88
Ázoe del ácido úrico	.174	.174	.174
Ázoe de las bases púricas	.096	.092	.094
Ázoe púrico total	.270	.5226	.268
Parte del ázoe amoniacal por 100 de ázoe total	10	6.99	8.49
Parte del ázoe de la urea por 100 de ázoe total	69.71	72.11	70.91

Promedios de Bogotá—Continúa.

	Clase obrera.	Clase acomodada.	Promedio s generales.
Parte del ázoe del ácido úrico por 100 de ázoe total	1.54	1.28	1.41
Parte del ázoe de las bases púricas por 100 ázoe total	.85	.68	.76
Parte del ácido úrico total por 100 de ázoe total	2.39	1.96	2.17
Fracción de ázoe determinado por 100	82.10	81.06	81.58
Fracción de ázoe indeterminado por 100	17.99	18.94	18.42
Índice de imperfección ureogénica por 100	12.54	8.85	10.69
Coeficiente de trasformación de los núcleoproteídeos por 100	64.43	65.3	I:64.82 II:62.90
Anhidrido fosfórico	1.91	1.97	1.94
Fósforo de los fosfatos	.76	.86	.81
Relación ponderal	14.85	15.80	15.82
Relación atómica	1:32.9	1:35	1:33.9

Promedios de Tunja.

Densidad	1014
Volumen en 24 horas	2548cc
Acidez (en H)	.068
Ázoe total	11.19
Amoniaco y ácidos aminados	.89
Urea	15.40
Purinas totales (en ácido úrico)	1.22
Ácido úrico	.56
Bases púricas (en xantina)	.229
Ázoe amoniacal	.75
Ázoe de la urea	7.10
Ázoe del ácido úrico	.18
Ázoe de las bases púricas	.11
Ázoe púrico total	.29
Parte del ázoe amoniacal por 100 de ázoe total	6.70
Parte del ázoe de la urea por 100 de ázoe total	63.44
Parte del ázoe del ácido úrico por 100 de ázoe total	1.62
Parte del ázoe de las bases púricas por 100 de ázoe total	.98
Parte del ázoe púrico total por 100 de ázoe total	2.60
Fracción de ázoe determinado por 100	72.74
Fracción de ázoe indeterminado por 100	27.26
Coeficiente de trasformación de los nucleoproteidos por 100, I	60.23
Coeficiente de trasformación de los nucleoproteidos por 100, II	60.07
Anhidrico fosfórico	1.86
Fósforo de los fosfatos	.81
Relación ponderal	21.22
Relación atómica	1:46.9

Promedios generales.

Densidad	1.016
Volumen en 24 horas	2.103
Acidez (en H)	.054
Ázoe total	11.81
Amoniaco y ácidos aminados	1.07
Urea	17.41
Purinas totales (en ácido úrico)	1.17
Ácido úrico	.54
Bases púricas (en xantina)	.27
Ázoe amoniacal	.89
Ázoe de la urea	7.99
Ázoe del ácido úrico	.096
Ázoe de las bases púricas	.102
Ázoe púrico total	.148
Parte del ázoe amoniacal por 100 de ázoe total	7.59
Parte del ázoe de la urea por 100 de ázoe total	67.17
Parte del ázoe del ácido úrico por 100 de ázoe total	1.51
Parte del ázoe de las bases púricas por 100 de ázoe total	.87
Parte del ázoe púrico total por 100 de ázoe total	2.38
Fracción de ázoe determinado	72.76
Fracción de ázoe indeterminado	22.84
Índice de imperfección ureogénica.	9.92
Coeficiente de trasformación de los núcleoproteidos por 100, I	62.52
Coeficiente de trasformación de los núcleoproteidos por 100, II	62.48
Anhidrido fosfórico	1.90
Fósforo de los fosfatos	.81
Relación ponderal	18.27
Relación atómica	36.56

Discusión de los Resultados Obtenidos.

Si se quiere sacar alguna enseñanza del cuadro de promedios de los noventa y seis análisis en general, de cada clase social en particular, es indispensable conocer el resultado de análisis hechos recientemente en Europa y tenidos allí como precisos.

La comparación posterior entre los resultados obtenidos en Bogotá y los obtenidos en Tunja, nos dará preciosas enseñanzas sobre el metabolismo azoado entre nosotros.

Antes de hacer comparaciones y como punto de partida, voy a permitirme trascribir el cuadro de resultados medios obtenidos por Maillard, el cual es considerado en Francia "como uno de los documentos más completos que se posee en la hora actual sobre la orina del hobre con régimen mixto, puesto que los análisis se hicieron por los procedimientos más precisos conocidos hasta entonces y que cada una de las cifras del cuadro representa el promedio de sesenta determinaciones." Tiene además, en el caso presente la inmensa ventaja de que los resultados fueron obtenidos casi en su totalidad y con ligeras variaciones, por los mismos métodos de análisis empleados por mí.

He aquí estos promedios de eliminación en veinticuatro horas:

Volumen	1.810	Parte del ázoe del ácido úrico por 100 de ázoe total	1.43
Acidez (en hidrógeno)	.045	Parte del ázoe de las bases púricas por 100 de ázoe total	.22
Amoniaco	1.11	Parte del ázoe silicotúgstico por 100 de ázoe total	.57
Urea	27.64	Fracción determinada de ázoe por 100	88.85
Purinas básicas	.10	Fracción indeterminada de ázoe por 100	11.15
Ázoe total	15.87	Anhidrido fosfórico	2.19
Ázoe amoniacal	.91	Fósforo de los fosfatos	.96
Ázoe de la urea	12.09	Relación atómica	1:37.9
Ázoe púrico total	.262		
Ázoe del ácido úrico	.227		
Ázoe de las bases púricas	.035		
Ázoe silicotúngstico	.090		
Parte del ázoe amoniacal por 100 de ázoe total	5.73		
Parte del ázoe de la urea por 100 de ázoe total	81.29		

Si se comparan estos resultados con mi cuadro de promedios se observan diferencias considerables en la mayor parte de las cifras: diferencias que no pueden atribuirse a errores de técnica porque, como ya dije, los análisis se hicieron por los mismos métodos que empleó Maillard y algunos procedimientos más precisos no conocidos en la época en que hizo sus análisis este distinguido fisiólogo. Además, los reactivos fueron titulados con el mayor escrupulo y usando medidas de las más precisas conocidas.

Analicemos separadamente: 1°. Los productos de desintegración albuminoidea. 2°. Los de desintegración núcleo proteica: (3°) ázoe total. (4°) ázoe indeterminado. (5°) fósforo. (6°) acidez.

I. *Productos de desintegración albuminoidea.*—Lo primero que llama la atención al hacer la comparación de los dos promedios es que hay en los míos una disminución de la urea (de 10.23) disminución más considerable que la encontrada por el Dr. del Río pues él encontró en algunos casos hasta 36 gramos en las 24 horas. Es posible que esta desproporción de cifras obtenidas en la misma localidad sea debida a que el Dr. del Río al medir la urea por el procedimiento gasométrico no eliminó—o no lo hizo hasta donde es posible hoy—las causas de error debidas a las variaciones de temperatura y de presión atmosférica así como las causadas por el ácido úrico, las bases púricas y el amoniaco.

Esta disminución de la excreción de la urea entre nosotros en parte relativa porque hay al mismo tiempo una disminución del ázoe total diferencia que es de 4.06 en las 24 horas. Pero se verá que la primera es también real si se compara la cifra

que representa la relación entre el ázoe de la urea y cien partes de ázoe total que es entre nosotros de 67.17 y en Europa 81.29 según Maillard: y según Desgrez y Aysignac, quienes se fundan en un gran número de análisis, es como sigue para los diferentes regímenes:

Régimen lácteo absoluto 86, régimen mixto (leche nuevos vegetales) 86, régimen mixto (lacto-vegetariano) 81, régimen mixto débilmente carneo, 82, régimen mixto (vegetariano absoluto) 78.

Comparando ahora los análisis de Tunja con los de Bogotá, observamos una diferencia en favor de éstos de 3.52 para la cifra de la urea y de 7.47 para la relación entre el ázoe total y la urea. Dato muy interesante que debe tenerse muy presente para las conclusiones de este estudio.

Es verdad que para dosar la urea emplee métodos diferentes de los del experimentador cuyos datos están sirviendo de comparación pues él empleó el de Folin en tanto que yo empleé el gasométrico; pero las causas de error de que adolece este último fueron corregidas en gran parte; por otra parte el error si existió debió ser por exceso por falta de una completa precipitación del ácido úrico y de las bases púricas; por último; existe el antecedente de la igualdad de los resultados obtenidos por Desgrez y Ayrignac con el método gasométrico y los de Maillard con el de Folin.

En cuanto al amoníaco, se observa, en los análisis de Bogotá un aumento de 0.15 con respecto al cuadro, lo que está de acuerdo con la disminución de la urea.

En los análisis de Tunja se observa al contrario una disminución; pero si en vez de tener en cuenta la sola cifra del amoníaco se considera la del ázoe amoniacal con relación al ázoe total, se verá que esta disminución no es sino aparente pues hay en favor de los análisis de Tunja, un aumento de 1.07 con relación al cuadro que sirve de patrón.

Hay pues siempre una relación, más o menos exacta entre la disminución de la urea y el aumento del amoníaco.

Es de notar que para medir el amoníaco empleé el procedimiento de Ronchese, con las mismas correcciones con que lo empleó Maillard.

Como se hace más patente esta diferencia, es comparando los índices de inperfección urogénica que son, según el cuadro del autor copiado arriba, de 6.58 por ciento. Aplicando el calculo a los análisis de Donze y Lambling, se encuentra 6.12.

Estas cifras varían según Lauzenberg[1] con el régimen alimenticio: El régimen lácteo da valores más débiles (4.28) y el carnos más fuertes (6.31). (Es decir menores que los obtenidos por Vaillard con régimen mixto). El vegetariano da valores medios (5.21).

Cualquiera que sea el valor que se atribuya a los resultados que menciono, es preciso observar que existe entre nosotros un aumento de este coeficiente, mucho mayor para las clases pobres que para las clases acomodadas. Y que el promedio de Tunja que se refiere a individuos más mal que bien alimentados, es mayor que el de la clase acomodada de Bogotá.

Es verdad que todavía no se cónocen bien las variaciones fisiológicas de este coeficiente, pero dada la desproporción que existe entre las cifras apuntadas y las obtenidas por mí, es preciso concluir que existe entre nosotros (y quizá un poco más en Tunja que en Bogotá) una imperfección en la transformación de las albuminoideas o sea una insuficiencia de la actividad global del organismo para el conjunto de estos tres fenómenos: separación reductiva o hidrolítica del amoníaco, oxidación de los ácidos grasos y deshidratación del carbonato de amoníaco, lo que se comprenderá fácilmente si se recuerdan las trasformaciones que sufren los aminoácidos que llegan hasta la urea; de aquí que este índice haya sido llamado también coeficiente de oxidación verdadero o de los ácidos grasos.

[1] Tesis de Paris, 1812.

Este aumento de la imperfección urogénica puede ser debido: a la calidad del régimen alimenticio, a una insuficiencia hepática, a una lentitud de las oxidaciones o del metabolismo en general, las qua a su turno pueden depender de otras tantas causas qua analizaré más adelante.

(a) El régimen carneo aumenta y el régimen vegetariano disminuye el coeficiente en cuestión: esto porque, como se vió atrás los ácidos, que se forman en el organismo, ácidos que resultan sobre todo de la desintegración de los albuminoideos animales, retienen fuertemente el amoniaco y le impiden seguir su transformación hacia la urea.

Entre nosotros no parece que se deba atribuir a esta causa el aumento del coeficiente 1° porque la observación nos enseña que nuestras clases acomodadas consumen mucha menos carne que la que se consume en los países latinos de Europa (menos carnívoros que los sajones).

Según se deduce de los autores que he podido consultar a este respecto, la cifra media de carne consumida por cada individuo en París es, como se verá más adelante, superior al máximum de nuestras clases acomodadas: (2°) Porque el aumento es mayor en las clases pobres cuya alimentación es especialmente vegetariana e hidrocarbonada y (3°) porque los mismos análisis de las orinas dejan ver que, al menos en Bogotá, no hay un aumento de la acidez pues esta cifra es inferior la obtenida por Maillard, lo que indicaría más bien un predominio del régimen vegetariano.

(b) Podría más bien pensarse en una insuficiencia hepática, teniendo en cuenta que el índice de imperfección urogénica es mucho mayor en nuestras clases trabajadoras las que, como se sabe ingieren una gran cantidad de alcohol en la chicha, bebida que constituye en muchos de estos individuos casi la totalidad su alimentación.

(c) Pero puesto que la cifra es también elevada en las clases acomodadas, fuerza es concluir que si la causa de que acabo de hablar existe o puede existir por la insuficiencia de la alimentación animal que obligaría a recargar las vías digestivas con un exceso de alimentos vegetales lo que sería causa de insuficiencia hepática hay otros datos consignados en el curso de este estudio que no podrían pasar inadvertidos como son: la baja de temperatura, de glóbulos rojos y de hemoglobina, lo que obliga a creer en una lentitud entre nosotros de todas las trasformaciones orgánicas quizá por insuficiencias glandulares que traen consigo insuficiencias de fermentos.

Ahora: llevando las cosas hasta donde es posible, al terreno de un régimen alimenticio semejante, podrían como ya dije, considerarse los sujetos de mis experimentos en Tunja como pertenecientes a la "clase obrera" de Bogotá.

Hay en aquéllos un aumento con relación a éstos, aumento que no estaría en relación con la ligera disminución de glóbulos rojos y de temperatura. Adelante se verá alguna explicación a este fenómeno, pero sería imprudente formular conclusión alguna dado el pequeño número de mis observaciones de Tunja con relación a los de Bogotá.

II. *Productos de desintegración núcleo proteidica: Índice de su transformación.*— Obsérvese que las cifras que representan el acido úrico y las bases púricas son casi idénticas en el cuadro de Bogotá (0.78) y en el de Maillard (0.77). Muy ligeramente aumentados en el de Tunja (0.81): lo que indica que la alimentación nucleo-proteica es casi la misma entre nosotros y los individuos que sirvieron de observación a Maillard. Pero hay más: comparando las dos cifras, en que están divididos los promedios de Bogotá se ve que casi son idénticas en la "clase obrera" y en la clase acomodada lo que, dada la diversidad de regímenes alimenticios, parece a primera vista inexplicable; pero si es verdad que nuestros obreros no consumen todo el café, el te y el cacao que consumen las clases acomodadas, consumen en cambio chicha, la que por sus levaduras da gran cantidad de purinas y por su alcohol y sus toxinas, destruye probablemente una gran cantidad de núcleoproteidas orgánicas.

Si se comparan las cifras que representan el porcentaje en relación con el ázoe total, se verá que nosotros ingerimos o destruimos una mayor cantidad de núcleo proteidas, en

relación con las albuminoideas. Pero a pesar de la igualdad de las cifras, el desacuerdo vuelve entre mis análisis y los que han servido de comparación con los europeos, si se divide la cifra de las purinas en sus dos factores: ácido úrico y bases púricas, hay para el primero un déficit en mis análisis de 0.16 en los análisis de Bogotá y de 0.12 en los de Tunja, y para la segunda un aumento de 0.17 en los de Bogotá y de 0.19 en los de Tunja.

Después de observar que mis análisis de estas sustancias fueron hechos por los mismos procedimientos que emplearon Donze y Lambling, Maillard y Boudrez con algunas variaciones respecto al ácido úrico por procedimientos más modernos y por un estudio detenido de los distintos métodos (veáse pág. 78–79) es preciso concluir que hay entre nosotros un aumento de los términos intermedios de la transformación de los núcleos proteidas, a expensas del término final de estas transformaciones; sucede, por consiguiente, algo muy semejante a lo que pasa con la desintegración de las albuminoideas con la sola diferencia de que en el caso presente (probablemente por la menor intervención del hígado) la diferencia no existe entre la clase acomodada y la clase obrera, pero al estudiar la relación, veremos que hay entre los análisis de Bogotá y los de Tunja, una diferencia en contra de éstos.

Queda pues, desde este punto de vista, justificado mi coeficiente de transformación de las núcleoproteidas que podría llamarse también de oxidación o de desamidación vistos los distintos grados de desintegración porque pasan estos cuerpos (véanse pág. 73 y siguientes).

Este coeficiente $\frac{\text{Az A. U.}}{\text{Az P. T.}}$

es, según mi cuadro de análisis de Bogotá, de 64.87 por ciento con una diferencia de 0.80 en favor de la clase acomodada y de 60.23 en los promedios de Tunja; es decir, que hay una diferencia en favor de Bogotá de 4.64.

Para poder juzgar del valor de este coeficiente, voy a hacer algunas comparaciones: aplicando el cálculo a los promedios de Maillard resulta 80.84 es decir una cifra que difiere de las mías (promedios generales) En 18.32 desigualdad muy proporcional a la que existe entre los índices de imperfección ureogénica.

Si en vez de tomar el porcentaje del ázoe total se toman las cifras directas de ázoe del ácido úrico y de purinas totales los resultados son naturalmente muy semejantes y dan: Cuadros de Tunja, 60.70; cuadros de Bogotá, 62.90. Cálculo aplicado a los resultados de Maillard, 86.64.

Esta segunda forma es la que se encuentra en los promedios marcada con el Número II.

Y, continuando las comparaciones: si se aplica ahora el cálculo a los resultados obtenidos por Bouchez [1]—quien hizo análisis de su propia orina—poniéndose diferentes regímenes de alimentación—se encuentran cifras un poco superiores a las de Maillard como se verá en seguida. Pero antes debo advertir que, para los promedios que copio, he tenido que prescindir de algunos análisis cuyos datos no tenía completos en el estudio mencionado:

Régimen mixto ordinario, 86.36; régimen mixto con nucha carne, 91.86; régimen lácteo, 91.02; alimentación disminuida, 84.05; régimen lácteo vegetariano rico en hidratos de carbono, 88.41.

Podría sacarse en conclusión de las cifras anteriores—que quizá por provenir de un individuo sujeto a un régimen alimenticio más rico que los sujetos en quienes experimentó Maillard dan cifras un poco superiores a éstas—que el régimen animal aumenta el valor del coeficiente y los regímenes vegetariano e hidrocarburados y la alimentación insuficiente lo disminuyen: enseñanzas que, al ser confirmadas con un mayor número

[1] A. Bouchez, Recherches sur la composition de l'urine normal de l'homme, Jour. de Phys. et de Path. Gén., enero 1912.

de observaciones, concordarían con los estudios hechos últimamente sobre las oxidasas de la carne y en general con el de las citadas de las albuminoideas de origen animal.

No puede negarse también que hay cierta proporción de diferencias con los análisis de Maillard y con los míos, entre el cuadro sacado de los estudios de Bouchez y el copiado anteriormente de Desgrez y Airignac referente este último a la relación entre la urea y el ázoe total.

Concordarían también los datos apuntados, con las observaciones de que hablé hace poco de las insuficiencia de la alimentación carnea en la altiplanicie de Bogotá alimentación que es casi nula en las clases pobres. Pasaría, en suma algo semejante a lo que pasa con el coeficiente de utilización del ázoe.

III. *Ázoe total* que es en el cuadro modelo 15.87, en mis promedios generales alcanza apenas a 11.81 y en los cuadros de Bogotá se nota una diferencia de 2.30 a favor de las clases acomodadas. Si, por un error imprevisto, no se hubiera hecho figurar entre los obreros a sirvientes, que, son por lo regular individuos bien alimentados, esta diferencia sería mucho mayor.

Las cifras apuntadas representan para los promedios generales, según los cálculos que quedaron anotados atrás (veáse pag. 57) de 73.71 de albúmina por cada individuo, o sean 353.81 caloría y en los cuadros de Bogotá: 77.75 de albúmina o 373.20 calorías para las clases obreras y de 84.94 de albúmina, o sean 407.71 calorías para las clases acomodadas.

Aplicando el cálculo a los análisis de Maillard se obtiene una diferencia en contra de mis sujetos de observación de 122.30 calorías. En cuanto a los análisis practicados en Tunja, se aproximan las cifras siendo inferiores a las de la clase obrera de Bogotá.

Queda pues demostrado, que hay entre nosotros un déficit de materiales albuminoideos aun en nuestras clases acomodadas.

IV. *Ázoe indeterminado por ciento de ázoe total.*—Entre todos los estudios que se han consultado no he encontrado otros, siquiera citados, a este respecto que los de Maillard y Dansé y Lambling y Bouchez. Los resultados del primero dan 11.15 por ciento y los de Dansé y Lambling 11.71; los de Bouchez dan una cifra muy inferior, en tanto que los míos dan: en los promedios generales 22.84, en los de Tunja 27.26, y en los de Bogotá 18.42, con un pequeño aumento para la clase obrera. La desigualdad de estos resultados se debe en primer lugar, a que los últimos de los autores citados, midieron la creatinina y el primero las bases precipitables por el ácido silicotúngstico sustancias que no figuran en mis análisis. Pero aun haciendo esta corrección hay siempre en mis promedios un aumento de la cifra en cuestión; veamos como puede ser explicado este aumento:

El ázoe indeterminado pertenece, sobre todo, a la creatinina a los ácidos uroproteicos (con el urocromo) al ácido hipúrico y a las bases precipitables por el ácido silicotúngstico. Recordemos algo sobre el origen de estos cuerpos.

1°. La creatinina es un hidrato de la creatina de la cual proviene, y este queda en libertad en la trasformación de muchas nucleo-proteidas en cuya composición entra,[1] de modo que habiendo un aumento de purinas, es natural que haya también un aumento de la creatinina y siendo ésta el principal factor de la fracción de ázoe indeterminado, podríamos de esta manera explicarnos el paralelismo entre el aumento de esta fracción y la de las purinas tanto en mis análisis con relación a los europeos, como en los de Tunja respecto a los de Bogotá.

Los vegetales contienen también creatina; de modo que el régimen vegetariano aumenta la proporción de la creatinina en las orinas.

2°. Cuando la dislocación de las albuminoideas es imperfecta, cuando el desdoblamiento o la desamidación de los ácidos aminados o la oxidación del ácido desaminado no es completa se encuentra en la orina mayor cantidad de ácido oxiproteico así como

[1] Professor C. H. Roger, Loc. cit. pág. 250.

de ácidos aloxiprotéico y urogénico [1] es decir que el aumento de estos ácidos está en razón directa del índice de imperfección urogénica.

3°. La orina de veinticuatro horas del hombre normal no contiene por término medio sino un gramo de ácido hipúrico (bajo forma de hipuratos). Los hipuratos son más abundantes en la orina de los herbívoros que en la de los carnívoros y estos aumentan con la alimentación vegetal. Sabiendo que el ácido benzoico entra en la síntesis del ácido hipúrico se comprenderá fácilmente la influencia del alimento vegetal en este aumento y si como ya lo insinué atrás y como se demostrará más adelante, nuestra alimentación es muy poco carnea y casi totalmente vegetariana tampoco sería raro que los hipuratos estuvieran en mayor proporción en la orina del hombre en la antiplanicie. Además, como la glicocola (que como se sabe es un ácido monoaminado de la serie alifática) entra también en la composición del ácido hipúrico, quizá pudiera explicarse, en parte, de esta manera, la correlación entre el aumento del ázoe indeterminado y la disminución de la urea con el régimen vegetariano. Si se tiene en cuenta la importante participación de los ácidos aminados en la formación de este último cuerpo.

No está por demás advertir que el ácido hipúrico es una de las sustancias cuya formación se atribuye a encimas de trabajo negativo es decir de cuya influencia resulta una reacción con absorción de calor. Encimas que operarían por consiguiente, según Duclux y Lambling, síntesis análogas a las de la granulación clorofiliana. La síntesis del ácido hipúrico parece que tenga lugar en el riñón.

4°. Ya dije todo lo que se sabe respecto a las bases precipitables por el ácido silicotúngstico. Respecto a sus variaciones en la orina, nada cierto se sabe hasta el presente.

Sería interesante averiguar cual de estos cuerpos que forman la cifra de ázoe indeterminado está en mayor proporción, desgraciadamente (quizá excluyendo uno o dos de ellos) no se conocen todavía procedimientos para medirlos exactamente.

5°. *Fósforo.*—En cuanto al fósforo de los fosfatos se encuentra una cifra idéntica en los análisis de Bogotá y en los de Tunja, a pesar de una ligera disminución en los promedios de estos últimos del anhidrido fosfórico. Comparando los promedios generales de mis análisis con el cuadro modelo, hay a primera vista una disminución en los primeros; pero si se relacionan estos resultados a los del ázoe total, hay al contrario, un aumento por lo cual la relación ponderal y la relación atómica son mayores en el cuadro adoptado como punto de comparación; la última relación es de 36.05 en mis promedios y 37.09 en el cuadro modelo.

Esto querría decir que mientras se elimina un átomo de fósforo se elimina entre nosotros una cantidad un poco menor de ázoe, lo que está de acuerdo con la mayor cantidad de purinas en relación con el ázoe total, pues se sabe que la mayor parte del fósforo urinario proviene de la desintegración de las nucleo-proteidas.

Esto último explicaría también por qué el fósforo está relativamente en mayor cantidad en los promedios de Tunja que en los de Bogotá.

6°. *Acidez.*—Hay un aumento de la acidez en los análisis de Tunja, probablemente porque estos análisis se refieren a individuos sujetos en su mayor parte a ejercicios musculares continuados y más carnívoros que a los que se refieren los análisis de Bogotá. En estos últimos hay una pequeña disminución, la cual podría ser atribuida al predominio de la alimentación vegetal; este aumento y esta disminución respecto de la acidez, son por lo demás muy pequeños para darles mayor importancia.

Como consecuencia final y resumen de estas interpretaciones, se desprende el hecho de que existe en la altiplanicie de Bogotá una insuficiencia de la utilización del ázoe tanto en la forma albuminoidea como en la nucleo-proteica, insuficiencia que se traduce en las orinas por un exceso de los términos intermedios del metabolismo a expensas de los términos finales; conclusión que concuerda con la baja de la temperatura y la disminución de la superficie hemoglobínica.

[1] Profesor E. Gley, Loc. cit.

Quiere esto decir que hay entre nosotros una inactividad en las trasformaciones orgánicas y especialmente en las oxidaciones.

¿A qué es debida esta inactividad?

Vimos atrás que el organismo animal no es como un horno cuya temperatura puede elevarse a voluntad con una mayor cantidad de combustible. De manera que si las combustiones bajan en personas que tienen recursos para proporcionarse toda clase de alimentos—siendo estos alimentos de composición química igual a los empleados en otras regiones como lo he demostrado por mis análisis—es forzoso concluir que, al menos el factor más importante de esta deficiencia de combustiones no es la cantidad de combustible sino se debe a otras causas que dependen probablemente de una degeneración fisiológica en los individuos.

Hay casi seguramente entre nosotros una disminución de los fermentos encargados de verificar estas trasformaciones y especialmente de oxidasas.

La insuficiencia de estos fermentos debe provenir de una falta de actividad de las glándulas encargadas de secretarlos: hipótesis que sería muy interesante confirmar y sobre la cual dejo adelantados los hechos demostrados con este estudio.

En un estudio muy bien elaborado y documentado que presentó el Dr. Luis Felipe Calderón al Segundo Congreso Médico Nacional, sobre sindromos poliglandulares en la antiplanicie y que fué justamente elogiado, llega entre otras a las siguientes conclusiones: (1°) Son frecuentes en la altiplanicie los sindromos poliglandulares y predominan en ella los causados por hipofunción; (3°) existe en la altiplanicie un infantilismo visceral hepático, de origen hipofisiario, compatible con la integridad funcional del hígado, pero que lo predispone a la insuficiencia y lo inhabilita para la superactividad que suscitan los climas cálidos; (5°) las cardiopatías de las menopausia, frecuentes en la altiplanicie, implican el tratamiento por la opoterapia ovariana.

Las causas de la disminución de la actividad orgánica pueden ser múltiples, sólo hablaré de tres, para no extenderme demasiado, que son en mi concepto las que merecen más atención; es la primera la influencia de la zona de que me ocuparé en las conclusiones, y las otras dos son ambas relacionadas con nuestras costumbres: la vida sedentaria y la clase de alimentación.

El hombre de la antiplanicie, sobre todo el hombre perteneciente a clase social un poco elevada, pasa su vida en una quietud casi absoluta y entregado a un ejercicio intelectual permanente y forzado. Desde muy temprana edad concurre a la escuela primaria, donde sólo se le dejan algunas horas de descanso, y el resto del día lo pasa en un recogimiento absoluto, dedicando muy poco o ningún tiempo para atender a desarrollo físico.

Nuestros colegios de educación secundaria son todos escasos de espacio y si en algunos de ellos se distrae algún tiempo para los juegos y la gimnasia no se les dedica el tiempo necesario ni se hacen con método. Por otra parte, todavía no se han aclimatado entre nosotros los métodos modernos de instrucción, con los cuales se aprende mucho y se trabaja poco intelectualmente: todavía se fatiga el cerebro de los jóvenes con una cantidad excesiva de estudios, muchos de los cuales están archivados por inútiles en todo país civilizado.

Y si esto se dice de los hombres otro tanto podría decirse de las mujeres en cuanto a la vida sedentaria se refiere.

De aquí que el Dr. Calderón diga en la última conclusión del estudio mencionado: "La higiene escolar de la altiplanicie debe velar por los progresos del desarrollo físico y proveer a su deficiencia con cambios de clima adecuados a la actividad fisiológica de las glándulas que lo rigen." [1]

A las conclusiones del Dr. Calderón sobre insuficiencias poliglandulares puedo agregar que en mi práctica de laboratorio he tenido ocasión de encontrar—en exámenes hechos para la compañías de seguros—azúcar en las orinas de individuos cuyo examen clínico no deja sospechas de perturbación de salud alguna.

[1] Libro del Segundo Congreso Médico Nacional Colombiano, 1913.

Sería interesante practicar a este respecto en individuos en aparente estado fisiológico, experimentos semejantes a los que, en enfermos, practiqué respecto de insuficiencia hepática, bajo la dirección del profesor Roberto Franco y que condensé en un estudio que fué enviado al Segundo Congreso Médico Nacional Colombiano.

Un hecho interesante en la alimentación consiste en que el habitante de Bogotá consume menos carne que un europeo, aun haciendo la comparación con países de raza latina que como se sabe son menos carnívoros que los sajones. En efecto según estadísticas citadas por Labbé,[1] cada habitante de París consume, por término medio, 260 gramos de carne en las veinticuatro horas; y por datos que he podido recopilar tanto en la Plaza de Carnes como en la Oficina de Higiene y Salubridad, se verá que en Bogotá este consumo es mucho menor.

En el año de 1912, año en que el consumo ha llegado al máximo, se expendieron en Bogotá, aproximadamente y por término medio, a razón de 1,188 arrobas por día, lo que corresponde para 120,000 habitantes a 124 gramos por persona. El máximum de este consumo no alcanza, según se ha podido averiguarlo, entre las clases acomodadas a 160 gramos por persona; es decir a igualar siquiera las cifras medias de París; y en la mayor parte de los trabajadores llega a cero.

Esto se debe, en parte, a la falta del uso entre nuestras clases pobres, de carnes baratas como las de caballo, etc., que tanto consumo tienen en Europa.

Pero hoy no alcanzaría a dar el promedio apuntado arriba, pues parece que cada día van haciendo más mella entre nosotros las teorías sobre culpabilidad del régimen carneo en la producción de la arterio-esclerosis y de la vejez prematura: así, el número de reses sacrificadas, que venía como en todas partes, aumentando con el aumento de la población, y que de 22,954 que fué en 1910 había llegado en una progresión no interrumpida, a 25,559 en 1912, no ha sido en el año de 1913 hasta fines del mes de junio sino de 11,530, es decir, que probablemente no alcanzará ni a 24,000 o sea a una cifra inferior a la del año anterior.

Yo sé de muchas familias bogotanas que han proscrito la carne de su alimentación, impresionadas por temores que muchos médicos contribuyen a fomentar, con lo cual hacen un grave mal en mi concepto. Pues si se exceptúan muchas enfermedades en las cuales debe prohibirse la carne por tiempo más o menos largo, todo ser humano necesita comer carne, y necesita comerla en mayor cantidad de la que entra en nuestra alimentación, como lo voy a demostrar:

El organismo necesita de albuminoideas; las causas de esta necesidad todavía no son bien conocidas, pero sí está bien demostrado que ellas existen.

Si se examinan los análisis de alimentos que figuran en el capítulo tercero, se verá que hay algunos vegetales, sobre todo entre las leguminosas, que contienen casi tantos materiales albuminoideos, como la carne. Pero las cifras dadas en estos análisis, como las dadas en todos los análisis de alimento, tienen el grave inconveniente de ser deducidas del ázoe total, procedimiento que como ya dije, no es exacto, porque hay en los vegetales otras materias azoadas (ácido azoico, amoníaco, creatina, etc.) que no son albuminoideas; de modo que para subvenir a sus necesidades de albúmina, tiene el organismo, a régimen vegetariano, que ingerir una gran cantidad de alimentos, lo que recarga en sumo grado las vías digestivas. Es quizá este uno de los motivos por los cuales casi todos los que van de aquí a Europa, notan que allí se come una mucho menor cantidad de alimento. "Además, la experiencia nos enseña," dice Roeser hablando de los vegetales ricos en albúmina[2] "que no podemos hacer uso sólo de éstos en muestra alimentación. Contienen una gran masa de cerulosa y además de que esta masa indigesta es nociva por su volumen hay que agregar que su presencia tiene respecto al jugo gástrico, un papel de inhibición. Un alimento albuminoideo debe presentarse al estado de pureza, es decir, desprovisto de sus envolturas menos atacables, para que sea fácilmente digerible, para que provoque una secreción gástrica útil.

[1] M. Labbé, les régimes alimentaires.

[2] P. T. Roeser, La chimie alimentaire, études de physiologie générale, 1905.

Hay que notar, además, que el almidón contenido en grandes proporciones en los vegetales, favorece en el intestino la pululación del bacilus amilobacter, agente de una fermentación ácida cuyos productos no quedan sin acción sobre la economía" y más adelante agrega: "Los despojos de la nutrición son numerosos aun cuando se haga uso de la carne, pero es preciso reconocer que en este último caso son menos nocivos." M. Bikel demostró en un estudio citado por Boruttau [1] que los procesos de putrefacción producidos en el intestino del perro son tanto más intensos cuanto más rica en vegetales sea la alimentación y que llegan al mínimun con el régimen carneo absoluto.

Por otra parte, la carne es el único alimento que tiene acción, específica sobre la secreción gástrica. Cuando se introduce en el estómago, evitando toda excitación psíquica, pan papilla de almidón y albúmina de huevo crudo o cocido, "estas sustancia se muestran inertes en presencia de la mucosa gástrica, y pueden permanecer así por varios días sin otra modificación que una fermentación pútrida.

"La mezcla de carne y de almidón, el caldo, el extracto de carne y con mayor razón la carne pura, provocan la aparición de un jugo dotado de un poder digestivo real y la digestión así comenzada se continúa automáticamente." [2] Este efecto muy notable es producido por una acción específica refleja sobre los centros nerviosos, y puede ser aprovechado con éxito para estimular el apetito de los convalecientes cuando la excitación psíquica inicial hace falta.

Pero hay una cuestión que interesa de modo más directo el hecho que se está tratando de interpretar y son los estudios hechos en estos últimos años sobre la importancia de la carne en el estímulo del metabolismo celular, por la presencia en ellos de fermentos activos, sobre todo de peroxidasas y de catalasas que no son destruidas por el calor. La leche contiene también muchos de estos fermentos; pero algunas razones referentes a la digestibilidad, la hacen menos recomendable. H. Busquet,[3] después de experimentos muy cuidadosos y muy interesantes, en los cuales alimentaba ranas, mantenidas en equilibrio ponderal, unas con carne de ranas otras con carne de vaca y otras con carne de cordero, dedujo que la ración de mantenimiento se realiza mejor en la rana, con la ingestión de carne de rana que con la de vaca o la de cordero, y que en las ranas en inanición, un aumento ponderal determinado se obtiene con un aporte de albúmina menor con la ingestión de una carne específica, que con la de carnes extrañas.

"Estas nociones nuevas relativas a la asimilación azoada permiten la comprensión fácil de hechos muy conocidos en le fisiología de la nutrición; la variabilidad de la necesidad de albúmina, según el alimento ingerido, se desprende, como consecuencia inmediata, de estos experimentos. Mientras la albúmina se aleja más de las albúminas específicas, mayor será la cantidad necesaria para el mantenimiento del equilibrio azoado." De modo que al tratar de mantener este equilibrio solamente con alimentos vegetales, sería ésta una causa más, agregada a las que ya mencioné atrás, para aumentar la ración alimenticia con perjuicio de las vías digestivas.

Las albúminas que más convienen al hombre son, en consecuencia, las que provienen de los mamíferos.

Estos datos concuerdan admirablemente con lo que a este respecto dice Ardelbalden sobre la cuestión de la necesidad de albúmina.

Si es verdad que la proteolisis digestiva consiste en una demolición, más o menos profunda, del edificio molecular de las albúminas, seguida, en la mucosa intestinal y quizá en el hígado, de una reconstitución en proteicas sanguíneas específicas, propias para determinado organismo, esta reconstrucción implica un primer desperdicio, que puede ser considerable. Esta reedificación debe hacerse, en efecto, por la ley del mínimum, es decir, que la proporción entre los diversos productos de la hidrolisis diges-

[1] H. Boruttau, Jour. de Phys. et Path. Gén., 1912, enero.

[2] Estracto publicado en el *Jurnal* citado, Tomo IX, 1907.

[3] Busquet, Contribution à l'étude de la valeur nutritive comparée des albumines étrangères et des albumines spécifiques chez la grenouille, Jour. de Phys. et de Path. Gén., 15 de mayo de 1909.

tiva que puede ser empleado en la reconstrucción del nuevo proteico, debe regularse según la cantidad de aquél cuyos fragmentos están en menor cantidad. Cuando luego las proteicas sanguíneas, así construidas, se ofrecen como alimento a las diversas especies que tienes necesidad de las materias azoadas, volverá a comenzar la misma operación de demolición y reconstrucción, naturalmente con un nuevo desperdicio."

Así se comprendería como, para hacer frente a la reconstrucción o al sostenimiento de esos protoplasmas, el organismo tiene necesidad de disponer de una cantidad considerable de albúmina, tanto más considerable cuanto más se aleje de las albúminas específicas.

Por último si la carne fuera nociva para el organismo, las razas sajonas no tendrían ya el vigor superior que conservan.

Si sólo el régimen carneo fuera la causa de la arterio-esclerosis, no existiría esta enfermedad en los mamíferos herbívoros.

En resumen: para una mejor utilización del ázoe alimenticio y una mejor marcha de las transformaciones orgánicas, el hombre necesita de una alimentación rica en albuminoideas animales especialmente en carne.

Pero no quiere esto decir que el régimen alimenticio humano deba ser solamente carneo. Hay en los vegetales, fuera de las materias azoadas, hidratos de carbono y sales minerales que son de suma utilidad; la celulosa misma contribuye, en gran manera, a mantener despejadas las vías digestivas, preparando así el campo para una mejor absorción.

El hombre no es un animal solamente carnívoro, como no es solamente herbívoro. La conformación misma de su aparato masticador, desde la disposición de su articulación témporo-maxilar hasta la forma y disposición de su sistema dentario, indican que está constituido para el régimen mixto. De modo que los que en estado fisiológico (entendiendo por fisiológico el organismo cuyas partes funcionan normalmente) pretendan someterse a un régimen absoluto, sea vegetariano o carneo, pecan contra la misma naturaleza.

Y continuando sobre el mismo tema de nuestro régimen alimenticio: tiene la chicha alguna influencia en el retardo de los procesos del metabolismo orgánico?

El asunto me ha parecido de tanta importancia que lo he hecho objeto de un estudio especial.

RESUMEN Y CONCLUSIONES.

En general, en un sujeto en buenas condiciones higiénicas las funciones de nutrición alcanzan un nivel normal, cualquiera que sea la cantidad de comburente de que disponga el organismo, y cualquiera que sea la temperatura atmosférica, a favor de ciertas funciones orgánicas de compensación (hiperglobulia o hiperhemoglobinuria y mayor frecuencia de la respiración y del pulso) y a favor de un aumento del combustible (alimentos).

Por otra parte parece demostrado:

I. Que en la altiplanicie de Bogotá la nutrición sufre un retardo el cual se revela:

1. Por un descenso de la cifra media de la temperatura humana.

2. Por una insuficiente transformación de los materiales azoados en el organismo, insuficiencia que se traduce a su turno.

(a) En una disminución de la relación entre el ázoe de la urea y el ázoe total.

(b) En un aumento del índice de imperfección ureogénica o de los ácidos grasos.

(c) En un aumento de los términos intermedios de transformación de los núcleoproteidos (bases púricas) a expensas del término final de estas mismas transformaciones (ácido úrico).

La relación que he encontrado entre este último fenómeno y los diferentes grados de nutrición me ha inducido a proponer un nuevo coeficiente urinario cuya explicación detallada se encuentra en diferentes capítulos de este trabajo.

(d) En un aumento de la cifra del Az indeterminado.

II. Este retardo de la nutrición no se debe a una disminución de combustible porque, además de que se encuentra tanto en las clases pobres como en las clases acomodadas,

una cantidad normal de ázoe en las orinas, se ve por los análisis que hice de los principios alimenticios, que éstos son por lo menos tan ricos en nuestra altiplanicie como en la zona templada.

Pero esto no excluye el que en las clases no acomodadas pueda tener influencia la insuficiencia de la alimentación y el uso de la chicha, bebida que parece ejercer una acción depresora sobre la nutrición general.

III. La causa de este retardo es probablemente una deficiencia orgánica en la elaboración de los fermentos encargados de verificar el metabolismo celular, especialmente de oxidasas. Y como se sabe que estos fermentos son elaborados por distintas glándulas del organismo, pudiéramos decir en otras palabras: insuficiencia poliglandular a este respecto.

IV. Todas estas manifestaciones de un retardo en la nutrición, parecen más bien aumentar que disminuir con la altura, como se ve por la comparación de las observaciones tomadas en Bogotá y en Tunja, ciudades de alturas un poco diferentes.

Pero¿ cuál es la causa eficiente de esta deficiencia orgánica?

El problema es demasiado difícil para poderle dar actualmente una solución y sería petulancia pretender hacer más que formular teorías más o menos aceptables y dejar que otros le den la solución satisfactoria.

Algunas consideraciones me inducen a creer que la causa en cuestión tiene una relación con la zona en que vivimos, entre ellas la observación hecha por todo viajero de la depresión volitiva de la apatía muscular de los habitantes de la zona intertropical.

Pero¿ cuál es esa causa? Teorías y teorías pueden emitirse.

Quizá no deje de tener alguna influencia la pobreza de nuestra alimentación en albuminoideos animales así como lo sedentario de nuestra vida; aunque esto último puede ser más bien efecto que causa.

Algunos creen que la falta del cambio de estaciones, la constante repetición de una misma sensación, enerva los sentidos e influye sobre la nutrición general, a la manera que una luz igualmente coloreada acaba por producir perturbaciones visuales e intelectuales o que la repetición del mismo manjar que no se cambia acaba por producir perturbaciones digestivas.

En alguna otra parte he leído la teoría de que la tierra en su movimiento de rotación acumula mayor cantidad de ácido carbónico en el ecuador, lo cual parece encontrar una confirmación en la diferencia de ácido carbónico, a favor de los trópicos, si se comparan análisis (como los del Profesor Lewy practicados en Bogotá) de la atmósfera intertropical con los de la zona templada.

Si esto es así, quizá pudiera este fenómeno darnos la explicación de porqué la vida vegetal adquiere mayor robustez en los trópicos y porque las razas animales degeneran allí.

"Porque el ácido carbónico," según Bobor, Hasselbaalch y Krogh, "influye sobre las oxidaciones orgánicas aun dentro de los límites fisiológicos." "Es," dice Burderman, "un depresor morboso," y pudiera ser, por su exceso entre nosotros, lo que Luciani llama "acciones permanentes que producen retardos en la nutrición."

Finalmente, ¿debemos considerar como consecuencia, o más bien como causa inmediata de esta insuficiente elaboración, la disminución de la superficie hemoglóbica, o sea la disminución del número de glóbulos rojos sin aumento de la carga hemoglobínica?

¿ iene el enrarecimiento del aire influencia sobre el retardo de nuestras combustiones? La respuesta categórica es demasiado difícil, pero se pueden hacer algunas anotaciones al rededor de ella.

Parece por una parte demostrado, en estudios experimentales hechos por distintos autores, que a medida que se asciende hay una hiperglobulia o hiperhemoglobinuria compensadora del enrarecimiento del aire.

Por otra parte, otras observaciones hechas en la zona tórrida, concuerdan con las mías en esta falta de compensación.

En efecto, el Dr. José G. Hernández de Caracas [1] encontró en aquella ciudad, 893 metros sobre el nivel del mar, un promedio en 25 individuos de 3,840,000 glóbulos rojos por milímetro cúbico.

Cuatro años después, el Dr. Jorge Vargas encontró en Bogotá en 33 observaciones un promedio muy semejante al mío y anotó la relación entre sus observaciones y las de Del Río sobre disminución de la urea, así como el descenso de la temperatura humana en Bogotá.

Esta falta de compensación trae como consecuencia un aporte menor de oxígeno y por consiguiente, una disminución de las oxidaciones.

Pero recuérdese que los autores que han encontrado la compensación han experimentado en individuos sometidos por corto tiempo a la influencia de la altura y que en extranjeros recién llegados a nuestra altiplanicie si se ha encontrado esta compensación.

Por otra parte, tanto los estudios de los doctores Hernández y Vargas como los míos, se refieren a individuos que han vivido la mayor parte de su vida en la altura o al menos en la zona tórrida.

Cualquiera diría que no se cumple en nosotros esta ley fisiológica puesto que falta la compensación de que hablo; pero *compensación* que implica en este caso *hiperfunción*—quiere decir aumento de trabajo y el aumento de trabajo trae consigo el cansancio precoz. ¿No podría suceder que a la manera como el corazón se fatiga más fácilmente en las grandes alturas, pudiera venir también una hipofunción de los órganos hematopoieicos, bajo la influencia prolongada de un aire enrarecido?

Además el oxígeno es un gran excitante de las funciones de nutrición como lo prueban sus excelentes resultados y los del aire puro en los enfermos con hiponutrición. De aquí que no sólo las oxidaciones se encuentren disminuídas en nosotros, sino casi todas las reacciones del metabolismo.

Ahora bien: existe en la zona templada, por lo menos durante medio año una doble condición que hace la atmósfera mucho más densa: *baja temperatura* y *bajo nivel* sobre el mar. Mientras que en nuestra zona tropical hay una condición permanente de encarecimiento: en las regiones frías por la altura y en las partes bajas por el calor.

He ahí, en mi concepto, una posible influencia favorable del cambio de estaciones, sobre las funciones del metabolismo celular.

Esta diferencia en la actividad del metabolismo explica por qué se siente menos intenso el frío en las zonas templadas—aun con estados higrométricos iguales y con temperaturas más bajas—y por qué, utilizándose mejor los principios alimenticios se ve más vida en los individuos aún con más pequeñas cantidades de alimentos.

En todo caso el hecho de la insuficiente nutrición entre nosotros parece demostrado; falta buscar la explicación y probarla experimentalmente.

Pero entre tanto algo puede hacerse para remediar el mal:

1. Dar grande importancia a la educación física de los niños, porque, como dice Bedict, "el trabajo muscular es un estímulo, no sólo inmediato sino sostenido de la actividad celular" y dar la preferencia a aquellos ejercicios que desarrollan la capacidad torácica.

2. Luchar contra el uso de la chicha.

3. Quitar de la mente del pueblo la idea de que la carne es perjudicial para el hombre sano, a fin de hacer la alimentación más rica en albuminoideos animales que son un gran estímulo de la nutrición general.

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[1] J. G. Hernández. The Number of the red cells. Pan American Medical Congress, 1895.

INFLUENCIA DE LA CHICHA SOBRE EL METABOLISMO AZOADO.

Por CALIXTO TORRES UMAÑA.

La chicha es la bebida ordinaria de nuestro pueblo; es una especie de cerveza que proviene de la fermentación del maíz pero hay dos circunstacias que hacen de ella una bebida infinitamente más nociva para el organismo que la cerveza.

Es la primera que el maíz no contiene sino menos de la mitad de la glucosa que encierra la cebada y la segunda que es muy difícil desarrollar en el grano el fermento que debe trasformar el almidón en azúcar. Por estas razones, la industria ha tenido que apelar a un procedimiento tan largo que convierte la fermentación en una verdadera putrefacción; pues además del alcohol tienen tiempo de desarrollarse otras sustancias mucho más nocivas que éste.

Debemos al ilustre profesor colombiano Dr. Liborio Zerda, el primero y más completo estudio de los diversos productos de fermentación a que da lugar el procedimiento que hoy se emplea para la preparación de la chicha.

"Este estudio lo hizo el Dr. Zerda hace ya cerca de 20 años y aunque," según lo hace notar muy juiciosamente el Dr. Pablo García Medina,[1] "en este espacio de tiempo la química biológica ha hecho grandes adelantos y modificado muchas teorías, fué este trabajo tan completo, privó en él un criterio tan seguro y un método tan rigurosamente científico que hoy parece hecho a la luz de esos adelantos."

Es en el último período de la fermentación de la chicha, período que puede llamarse de putrefacción, cuando se desarrolla una tomaina que encontró el Dr. Zerda.

El Dr. F. J. Tapia lo ha demostrado de una manera muy sencilla. Toma un poco de maíz, suficientemente reblandecido para que pueda formarse lo que se ha llamado mazato, cuyo verdadero olor está casi oculto por el de los éteres que se desarrollan simultáneamente. Calentando este mazato, de manera que los éteres se evaporen, queda una masa de olor pútrido intenso como de cadáver en descomposición, lo cual da una idea de las diversas alteraciones que sufrirá el maíz durante este último período de verdadera putrefacción.

He aquí la composición de la chicha, al terminarse esta fermentación, según los análisis del Dr. Zerda:

	Gramos.		Gramos.
Alcohol	65.00	Almidón	10.80
Acido láctico	4.30	Materias azoadas	6.27
Otros ácidos	1.85	Glicerina	7.70
Azúcar (sacarosa, glucosa y azúcar invertida)	10.65	Aceite que contiene la sustancia tóxica	1.60

Pero la chicha así compuesta no se da al consumo sino mezclada con agua y miel, con lo cual se forma un líquido que por sufrir la fermentación alcohólica viene a quedar con mayor cantidad de alcohol que el primero pero con mucho menos sustancias nutritivas.

En tres litros de chicha que, más o menos, consume un trabajador de la sabana de Bogotá, hay 340 gramos de alcohol es decir como si tomara media botella de aguardiente más una gran cantidad de los elementos tóxicos propios de la chicha.

Las alteraciones especiales que produce la chicha en el organismo, estudiadas por el Dr. José Gomez[2] alteraciones distintas de las del alcoholismo ordinario, y que son casi idénticas a las de la pelagra; los experimentos practicados por el Dr. Zerda en animales y el análisis mismo de la chicha, me hicieron pensar que esta bebida puede tener alguna influencia inmediata en el retardo de la nutrición de nuestro pueblo de la altiplanicie.

Con el objeto de investigar esta influencia me dirigí al Ministerio de la Guerra para solicitar que se pusieran a mi disposición seis individuos de tropa y tuve la fortuna

[1] Sesiones científicas del centenario de Colombia, 1910. [2] José Gomes, el chichismo.

de ser debidamente atendido tanto por el Señor Ministro como por el Sr. Coronel Balcázar, Jefe de la Guarnición de Tunja, y por el Dr. Acevedo, oficial de sanidad de la misma, quienes contribuyeron en gran manera a que los experimentos se llevaran a cabo con absoluta precisión.

En la única parte en donde estos ensayos pueden llevarse a cabo con la absoluta exactitud que el caso requiere, es en el cuartel donde los sujetos están sometidos a una rigurosa disciplina y por consiguiente observan exactamente el régimen y las instrucciones bajo la vigilancia de sus superiores.

Para hacer mis investigaciones emplee un método semejante al que empleó el Profesor Maillard en el ejército francés, cuando estudió la influencia del vino sobre la excreción del ázoe y del fósforo.

Elegí seis sujetos bien conformados, en buen estado de salud y entregados a su vida ordinaria de cuartel.

Todos se sometieron a un régimen constante que observaron cada uno seis días, divididos éstos seis días en dos períodos de a tres: en el segundo período agregaron a su alimentación 200 c. c. de chicha al almuerzo y otros 200 a la comida.

Como por lo demás el régimen era exactamente el mismo, las variaciones que se observaran en este último período representarían la influencia de la chicha en la eliminación urinaria; pero como esta bebida tiene cierta cantidad de materiales azoados los individuos ingerían éstos en mayor proporción, dato que debe tenerse en cuenta al hacer la comparación de los promedios.

Como era imposible practicar seis análisis de orinas completas en menos de cuatro o cinco días, resolví, para que no se produjera una fermentación de las orinas que alteraría los resultados, dividir los sujetos en dos grupos, cada uno de los cuales se sometió durante los seis días al mismo régimen no sólo alimenticio sino de ejercicios (estos eran los ordinarios del cuartel sin salir al terreno).

El régimen alimenticio era el siguiente, es decir casi el ordinario del cuartel:

Desayuno: Agua de panela, 300 c. c.; pan de munición, 90 gramos. Almuerzo: Sopa, 1.500 c. c.; carne, 60 gramos; pan, 45 pramos. Comida: Mazamorra, 1.500 c. c.; carne, 60 gramos; papas, 960 gramos; panela, 90 gramos. Lo que da por día y por individuo las siguientes cantidades de materiales utilizables:

Alimentos.	Cantidades por hombre.	Materias proteicas.	Grasas.	Hidratos de carbono.
	Gramos.			
Panela	110	.....	.....	99.00
Pan	135	8.70	0.19	75.20
Carne	130	22.32	23.35	.....
Maíz	150	16.75	6.00	2.85
Papas	960	16.60	9.60	192.00
Total	.....	64.37	39.14	368.85

Estos cálculos han sido deducidos de mis análisis personales de alimentos, cuyos resultados son casi idénticos a los de Band y a los de Alquier.

Si se quiere conocer la cantidad de energía puesta a disposición del organismo por esta ración, hay que multiplicar cada uno de estos elementos por los coeficientes caloríficos: he aquí el valor de la ración:

Materias proteicas	64.37×4.4=	283.23
Grasas	39.14×9.4=	367.92
Hidratos da carbono	368.85×4.1=	1,512.29
Total de calorías		2,163.44

Los análisis de las orinas han sido practicados por los mismos procedimientos y con las mismas precauciones de los análisis del estudio sobre *Nutrición en Bogotá.*

Los cuadros que se verán en seguida representan para cada individuo el promedio de los tres análisis de cada período y al fin de cada serie de cuadros se encontrarán los dos promedios generales que servirán de comparación: el del período de abstención de chicha y el del período de chicha.

Las orinas fueron recogidas con todas las precauciones necesarias para impedir la fermentación amoniacal y además, para mayor seguridad se medía la acidez tanto a su llegada al Laboratorio como en el momento del análisis; este se principiaba por aquellas sustancias más fáciles de descomponer.

Período de abstención de chicha—eliminación del ázoe.

Núm.	Años de edad.	Temperatura.	Pulso.	Respiraciones.	Densidad de la orina.	Volumen en 24 horas.	Acidez en H.		Ázoe total.	
							Por litro.	En 24 horas.	Por litro.	En 24 horas.
1	24	36.6	88	20	1,015	2,900	0.027	0.78	4.13	11.95
2	22	36.6	84	18	1,010	2,800	.013	.036	2.06	5.77
3	21	36.7	74	18	1,016	2,450	.022	.054	2.94	7.20
4	21	36.5	82	20	1,012	3,300	.021	.069	3.33	10.99
5	22	36.9	76	19	1,014	3,150	.021	.066	3.80	11 97
6	22	37.0	78	20	1,015	29,502	.023	.068	4.10	12.09

Núm.	Amoníaco y ácidos aminados.		Urea.		Purinas totales (en ácido úrico).		Acido úrico.		Bases púricas (enxantina).		Acido fosfórico.	
	Por litros.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.
1	0.24	0.70	4.86	13.93	0.44	1.27	0.31	0.90	0.059	0.171	0.90	2.61
2	.20	.56	3.43	9.60	.41	1.16	.23	.64	.081	.179	.60	1.68
3	.20	.49	4.86	11.81	.55	1.59	.32	.82	.104	.255	.60	1.47
4	.27	.89	4.71	15.54	.45	1.48	.11	.36	.151	.508	.45	1.49
5	.23	.72	5.10	16.06	.45	1.45	.20	.63	.114	.359	.50	1.58
6	.20	.59	4.90	14.46	.42	1.24	.18	.53	.109	.322	.80	2.36

Período de abstención de chicha—eliminación del ázoe y relación del fósforo al ázoe (Cuadro I).

Números.	1	2	3	4	5	6
Ázoe amoniacal	0.58	0.46	0.39	0.73	0.59	0.49
Ázoe de la urea	6.41	3.31	5.92	7.26	7.51	6.75
Ázoe ácido úrico	.30	.21	.23	.12	.21	.18
Ázoe de las bases púricas	.062	.065	.093	.185	.131	.118
Ázoe púrico total	11.95	5.77	7.20	10.99	11.97	12.09
Part. del Az. amoniacal por 100 de ázoe total	4.85	7.80	5.36	6.64	4.97	4.05
Part. del Az. de la urea por 100 de ázoe total	52.89	57.37	82.22	66.05	65.26	55
Part. del Az. del ácido por 100 de úrico total	2.61	3.64	4.55	1.09	1.75	1.49
Part. del Az. de las bases púricas, por 100 de ázoe total	.52	1.12	1.29	1.68	1.18	.98
Part. del Az. púrico total, por 100 de ázoe total	3.13	4.76	5.84	2.77	7.93	2.47
Fracción de Az. determinado por 100	60.87	69.93	93.42	75.46	73.16	60.52
Fracción de Az. indeterminado por 100	39.13	30.07	6.58	24.54	26.84	39.48
Anhidrido fosfórico	2.61	1.49	1.47	1.49	1.58	2.36
Fósforo de los fosfatos	.93	.65	.64	.65	.69	.63
Relación ponderal	12.85	8.88	11.25	16.91	17.35	11.72
Relación atómica	28.4	12.3	24.9	37.4	35.3	25.9

Período de chicha—eliminación del ázoe y de purina.

Núm.	Años de edad.	Temperatura.	Pulso.	Respiraciones.	Densidad de la orina.	Volumen en 24 horas.	Acides en h.		Ázoe total.	
							Por litro.	En 24 horas.	Por litro.	En 24 horas.
1	24	36.2	88	20	1,008	2,100	0.018	0.055	3.81	11.81
2	22	36.4	82	17	1,010	3,240	.021	.068	2.86	9.15
3	21	36.5	72	18	1,014	3,020	.022	.066	4.44	13.40
4	21	36.6	76	19	1,011	2,900	.026	.065	4.84	14.04
5	22	36.3	76	19	1,014	3,200	.021	.067	4.20	15.44
6	22	36.7	74	20	1,012	3,000	.024	.072	4.60	13.80

Núm.	Amoníacos y ácidos aminados.		Urea.		Purinas totales en ácido úrico.		Ácido úrico.		Bases púricas (en xantina).		Ácido fosfórico.	
	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.	Por litro.	En 24 horas.
1	0.21	0.65	5.71	16.03	0.42	1.30	0.28	0.87	0.063	0.195	0.70	2.17
2	.31	1.00	3.43	11.11	.45	1.45	.19	.62	.118	.382	.60	1.94
3	.44	1.33	5.14	15.42	.22	.66	.11	.33	.048	.145	.40	1.20
4	.58	1.68	5.57	16.15	.46	1.33	.26	.75	.091	.201	.40	1.20
5	.48	1.53	4.80	15.36	.48	1.53	.18	.58	.091	.291	.80	2.56
6	.24	.72	5.00	15.00	.44	1.32	.15	.45	.132	.396	.90	2.70

Período de chicha—Repartición del ázoe y relación del fósforo al ázoe.

Números.	1	2	3	4	5	6
Ázoe amoniacal	0.54	0.82	1.09	1.38	1.26	0.59
Ázoe de la urea	7.49	5.19	7.19	7.54	7.17	7.07
Ázoe del ácido úrico	.26	.20	.11	.25	.19	.15
Ázoe de las bases púricas	.070	.139	.053	.072	.106	.263
Ázoe púrico total	.330	.339	.163	.322	.296	.413
Ázoe total	11.81	9.15	13.40	14.04	13.44	13.80
Parte del ázoe amoniacal por 100 de AzT	4.57	8.96	8.13	9.83	9.37	4.23
Parte del ázoe de la urea por 100 de AzT	63.42	56.72	53.73	53.53	53.34	51.23
Parte del ázoe del ácido úrico por 100 de AzT	2.20	2.21	.82	1.85	1.41	1.09
Parte del ázoe de las bases púricas por 100 de AzT	.593	1.508	.395	.513	.790	1.18
Parte del ázoe púrico total por 100 de AzT	2.793	3.718	1.21	2.36	2.20	2.27
Fracción de ázoe determinado	70.78	69.39	74.07	65.72	64.91	57.73
Fracción de ázoe indeterminado	29.22	30.61	25.93	34.28	35.09	42.27
Anhidrido fosfórico	2.17	1.94	1.20	1.20	2.56	2.70
Fósforo de los fosfatos	.94	.85	.52	.52	1.12	1.18
Relación ponderal	12.56	10.76	25.77	27.38	12.00	11.69
Relación alómica	27.8	23.8	57.00	60.6	26.57	25.9

PROMEDIOS.

I. Período de abstención de chicha:	
Densidad	1.013
Volumen en 24 horas (c. c.)	2.925
Acidez	.061
Ázoe total	10.41
Amoníaco y ácidos aminados	.70
Urea	13.20
Purinas totales	1.32
Ácido úrico	.67
Bases púricas	.270

I. Período de abstención de chicha—Continúa:	
Anhidrido fosfórico	1.87
Ázoe amoniacal	.58
Ázoe de la urea	6.16
Ázoe del ácido úrico	.25
Ázoe de las bases púricas	.161
Ázoe púrico total	.41
Parte del ázoe amoniacal por 100 de ázoe total	5.57
Parte del ázoe da la urea por 100 de ázoe total	59.03

PROMEDIOS—continúa.

I. Período de abstención de chicha—Continúa:	
Parte del ázoe ácido úrico por 100 de ázoe total.....	2.04
Parte del ázoe de las bases púricas por 100 de ázoe total.....	1.05
Parte del ázoe púrico total por 100 de ázoe total....	3.09
Fracción de ázoe determinado por 100.....	67.64
Fracción de ázoe indeterminado por 100.....	32.36
Fósforo de los fosfatos.....	.81
Relación ponderal.....	12.85
Relación atómica.....	1:28.5
Índice de imperfección urogénica.....	8.71
Índice de transformación de los núcleo proteidos.....	60.09
II. Período de chicha:	
Densidad.....	1.011
Volumen en 24 horas.....	3.076
Acidez.....	.055
Ázoe total.....	12.60
Amonfaco y ácidos aminados.....	1.15
Urea.....	14.84
Purinas totales.....	1.26
Ácido úrico.....	.60
Bases púricas.....	.30

II. Período de chicha—Continúa:	
Anhidrido fosfórico.....	1.96
Ázoe amoniacal.....	.95
Ázoe de la urea.....	6.93
Ázoe del ácido úrico.....	.20
Ázoe de las bases púricas.	.11
Ázoe púrico total.....	.31
Parte del ázoe amoniacal por 100 de ázoe total...	7.39
Parte del ázoe de la urea por 100 de ázoe total....	55
Parte del ázoe del ácido úrico por 100 de ázoe total.....	1.59
Parte del ázoe de las bases púricas por 100 de ázoe total.....	.87
Parte del ázoe púrico total por 100 de ázoe total....	2.46
Fracción de ázoe determinado por 100.....	64.85
Fracción de ázoe indeterminado por 100.....	35.15
Fósforo de los fosfatos.....	.86
Relación ponderal.....	15.06
Relación atómica.....	33.34
Indice de imperfección urogénica	10.20
Indice de transformación de los núcleo proteidos.....	57.92

DEDUCCIONES DE LOS PROMEDIOS.

Comparando los promedios, de los dos períodos vemos que hay en los segundos (período de chicha) con relación a los primeros, no dando mayor importancia a la pequeña baja de temperatura:

Una disminución de la densidad de la orina, de la acidez, del ácido úrico, del ázoe de la urea en relación con el ázoe total; del ázoe del ácido úrico, y del de las bases púricas con relación al ázoe total, del ázoe determinado y del índice de trasformación de los núcleos proteidos.

Un aumento: del volumen de la orina, del ázoe total, del amoníaco, de las bases puricas, del anhidrido fosfórico, del ázoe amoniacal con relación al ázoe total, y de la imperfección urogénica.

Nada más elocuente que estos resultados para establecer la conclusión franca, de que la chicha produce una inhibición sobre los procesos nutritivos.

Esta influencia retardante, quizá no sea debida al alcohol por la pequeña cantidad que ingirieron los sujetos de mis experimentos, porque no se verificaron los cambios en el pulso y en la respiración que producen pequeñas cantidadas de alcohol, y porque el Profesor Maillard tuvo que concluir un trabajo semejante al mío, con el dicho vulgar de que un vaso de vino no hace daño.

No sucede lo mismo con el vaso de chicha, la cual debe muy probablemente su acción retardante sobre la nutrición, a la tomaina descubierta por el Dr. Zerda y que a la manera del fósforo del óxido de carbono, del arsénico, de la morfina, etc.,

determina variaciones inmediatas en el funcionamiento químico normal del organismo en los procesos de nutrición general, y por consiguiente, en las excreciones urinarias en particular.

No tengo la pretensión de creer que mis resultados sean de una infalibilidad absoluta, pero sí que los experimentos han sido hechos con el más escrupuloso cuidado y por los mejores procedimientos hasta hoy conocidos.

Es esta una prueba más de que la chicha es un veneno y de que el Gobierno debe propender por cuantos medios estén a su alcance para impedir su uso.

Si es verdad que todos los ejércitos usan el alcohol a dosis moderadas como alimento energético (el aguardiente en Rusia, el vino en Francia y España, la cerveza en Alemania, etc.) debería elegirse para nuestros soldados una chicha en que la fermentación no llegara al estado de putrefacción a que generalmente llega, o una cerveza barata. De esta manera el cuartel sería una escuela para enseñarles a los hombres de nuestro pueblo, ya que no a dejar la bebida, cosa punto menos que imposible, al menos a cambiarla por una menos dañosa y a hacer uso de otras sustancias alimenticias, derivadas también del maíz, pero no dañosas como la chicha.

The CHAIRMAN. It is very difficult to follow this paper into all the complete details that are given. He brings into the paper evidence of nutritive retardation in the highland of Bogotá. Body temperature is lower. The amount of urea in the urine is less. The number of red cells, instead of being increased, as it is stated to be in the highlands, is diminished in that table-land of Bogotá. The pulse is somewhat accelerated and the respiration also, as a sort of compensatory respiratory and circulatory function. There is, therefore, a diminution of exudation of nitrogen and the utilization of nitrogen also. He believed for a time this might be due to the difference in the composition of the foods, since the nitrogen components of foodstuffs were found to be less than in other climates. He found that this was not so; that the composition of foods in the table-land of Colombia is exactly the same as in the Temperate Zones. As a side issue, but working in the same direction, he investigated the action of the common beverage of the country, chicha, of which he spoke when the question of pellagra came up, and he finds that this chicha, an alcoholic beverage from the fermentation of maize, exerts also evidently a retarding action upon this nutritive function, which he thinks may be due to the action of the ptomaine it was found to contain by one of his colleagues.

I do not quite understand his theory of this retarding function. One of his points (there are two) I understood well. He believes, suggesting without giving it as a positive opinion, that the rapid rotation of the earth increases the amount of carbonic acid in the atmosphere in the Tropics, thus causing this retardation of nutritive function. The other point is the absence of seasonal changes; that is, that there is a monotony in the landscape, a monotony in everything about, that in the same manner there is a monotony of light, a monotony of sound, which may produce serious disturbance in the nervous system.

The CHAIRMAN. The following papers, largely previously presented conference papers, have been courteously submitted to Section VIII by their writers. As a matter of record they will be included in the proceedings of the section:

Tratamiento de la coqueluche, by Rodolfo Kraus.

Ingerto testicular, by Antonio F. Celesia.

Vacunoterapia de la conjuntivitis granulosa, by E. B. Demaría, Salvador Mazza, y Hector Rebay.

Tratamiento de las apendicitis agudas, by Enrique J. Corbellini.

The CHAIRMAN. I beg to state that through the courtesy of the authors the following printed pamphlets have been presented to the Congress through Section VIII:

Investigaciones sobre el cultivo de la rabia por el método de Noguchi, by R. Kraus and B. Barbará. Las Ciencias, Librería y Casa Editora de A. Guidi Buffarini, Buenos Aires.

El carbón animal en la terapéutica y en la higiene, by R. Kraus and B. Barbará. Las Ciencias, Librería y Casa Editora de A. Guidi Buffarini, Buenos Aires, 1915.

Terapéutica heterobacteriana, by R. Kraus and S. Mazza. Las Ciencias, Librería y Casa Editora de A. Guidi Buffarini, Buenos Aires, 1914.

Contribución al estudio del tratamiento operatorio de los quistes uniloculares voluminosos y extrasinusales del maxilar superior, by Diogenes Massa. Talleres Gráficos de Juan Perrotti, Buenos Aires, 1915.

Profilaxia de la tifóidea por la vacunación en la República Argentina, by Salvador Mazza. Las Ciencias, Librería y Casa Editora de A. Guidi Buffarini, Buenos Aires, 1915.

Adjournment at 1.20 p. m.

GENERAL SESSION OF SECTION VIII.

NEW EBBITT HOTEL,
Monday afternoon, January 3, 1916.

Chairman, J. D. GATEWOOD.

The session was called to order at 2 o'clock, by the chairman.

The following papers were presented:

Changes in the food supply and their relation to nutrition, by Lafayette B. Mendel.

A safe and sane milk supply, by John Weinzirl.

Proyecto de ordenanza reglamentaria del comercio de leche de consumo en Buenos Aires, by Ricardo Sarmiento Laspiur.

CHANGES IN THE FOOD SUPPLY AND THEIR RELATION TO NUTRITION.

By LAFAYETTE B. MENDEL,
Professor of Physiological Chemistry, Sheffield Scientific School, Yale University.

In the type of civilization with which we are most familiar there are two fundamental elements—supplies of food energy and supplies of mechanical energy. Since, at present, partly because of geographical conditions, these do not necessarily (or even in general) occur together, there is a third essential factor, the line of transport.[1]

A comprehensive consideration of any one of these factors, such as the food supply, can not be completely dissociated from its relations to the others. The development of commerce among nations having adequate means of communication has, for example, rendered the distribution of food materials easy and developed a sense of security (under normal conditions) against failure of food supplies. The growing organization of transportation facilities has encouraged the introduction of dietary changes never thought possible or even contemplated a few generations ago. Incidents associated with the altered distribution of wealth have improved the nutrition as well as other conditions of living among that large group of our population which has been termed the "healthier well-to-do classes."

The supply of food energy and its availability where needed are interrelated closely with a variety of factors, the bearing of which upon the problem at hand is not always evident upon the surface. Some of these features may be classified superficially as follows:

1. Food production.
2. Food preservation and food conservation.
3. Transportation facilities.
4. Customs in diet.
5. Changing industrial and social conditions, and other economic and hygienic factors.

[1] Dickson, H. N.: The Redistribution of Mankind. Presidential Address to Section E (Geography) at the Birmingham meeting of the British Association, September, 1913. Report British Association for the Advancement of Science, Birmingham 1913, pp. 536-546. London 1914.

Food production.—The problem of food production is the fundamental concern of agriculture. How profoundly its practices are being changed by the progress of science and the mechanic arts is familiar to every observant person. The food supply has been increased in part through more intensive methods of agriculture, in part through the enormous extension of areas suitable for cultivation. In view of the increase of population it has been a favorite pastime for scientists to calculate the possibilities of the food supply of the future and to venture prophesies involving the prospect of impending failures. A forecast by Sir William Crookes of the relatioms between the probable increase of the world's supply and demand of wheat, "the most sustaining food grain of the great Caucasian race," was widely discussed when his estimates were published. In a Presidential Address to the British Association for the Advancement of Science in 1898 Crookes said:

Should all the wheat-growing countries add to their (producing) area to the utmost capacity, on the most careful calculation the yield would give us only an addition of some 100,000,000 acres, supplying, at the average world yield of 12.7 bushels to the acre, 1,270,000,000 bushels, just enough to supply the increase of population among bread eaters till the year 1931. * * * Thirty years is but a day in the life of a nation. Those present who may attend the meeting of the British Association 30 years hence will judge how far my forecasts are justified.

Fifteen years later Prof. Dickson said:

Half the allotted span has now elapsed, and it may be useful to inquire how things are going. Fortunately, this can be easily done, up to a certain point, at any rate, by reference to a paper published recently by Dr. J. F. Unstead, in which comparisons are given for the decades 1881–1890, 1891–1900, and 1901–1910. Dr. Unstead shows that the total wheat harvest for the world may be estimated at 2,258,000,000 bushels for the first of these periods, 2,575,000,000 for the second, and 3,233,000,000 for the third, increases of 14 per cent and 25 per cent, respectively. He points out that the increases were due "mainly to an increased acreage," the areas being 192,000,000, 211,000,000, and 242,000,000 acres, but also "to some extent (about 8 per cent) to an increased average yield per acre, for while in the first two periods this was 12 bushels, in the third period it rose to 13 bushels per acre."

If we take the period 1891–1900, as nearly corresponding to Sir William Crookes's initial date we find that the succeeding period shows an increase of 658,000,000 bushels, or about half the estimated increase required by 1891, and that attained chiefly by "increased acreage." But signs are not wanting that increase in this way will not go on indefinitely. We note (also from Dr. Unstead's paper) that in the two later periods the percentage of total wheat produced which was exported from the United States fell from 32 to 19, the yield per acre showing an increase meanwhile to 14 bushels. In the Russian Empire the percentage fell from 26 to 23, and only in the youngest of the new countries—Canada, Australia, and Argentina—do we find large proportional increases. Again it is significant that in the United Kingdom, which is, and always has been, the most sensitive of all wheat-producing countries to variations in the floating supply, the rate of falling off of home production shows marked if irregular diminution.

Looking at it in another way, we find (still from Dr. Unstead's figures) that the total amount sent out by the great exporting countries averaged in 1881–1890, 295,000,000, bushels; 1891–1900, 402,000,000; 1901–1910, 532,000,000. These quantities represent, respectively, 13, 15.6, and 16.1 per cent of the total production, and it would appear that the percentage available for export from these regions is, for the time at least, approaching its limit—i. e., that only about one-sixth of the wheat produced is available from surpluses in the regions of production for making good deficiencies elsewhere.

There is, on the other hand, abundant evidence that improved agriculture is beginning to raise the yield per acre over a large part of the producing area. Between the periods 1881–1890 and 1901–1910 the average in the United States rose from 12 to 14 bushels; in Russia, from 8 to 10; in Australia, from 8 to 10. It is likely that in these last two cases at least a part of the increase is due merely to more active occupation of fresh lands as well as to the use of more suitable varieties of seed, and the effect of improvements in methods of cultivation alone is more apparent in the older countries. During the same period the average yield increased in the United Kingdom from 28 to 32 bushels, in France from 17 to 20; Holland, 27 to 33; Belgium, 30 to 35; and it is most marked in the German Empire, for which the figures are 19 and 29.

In another important paper Dr. Unstead has shown that the production of wheat in North America may still in all likelihood be very largely increased by merely

increasing the area under cultivation, and the reasoning by which he justifies this conclusion certainly holds good over large districts elsewhere. It is of course impossible, in the present crude state of our knowledge or our own plant, to form any accurate estimate of the area which may be the use of suitable seeds or otherwise, become available for extensive cultivation. But I think it is clear that the available proportion of the total supply from "extensive" sources has reached, or almost reached, its maximum, and that we must depend more and more upon intensive farming, with its greater demands for labor.

The average total area under wheat is estimated by Dr. Unstead as 192,000,000 acres for 1881–1890, 211,000,000 acres for 1891–1900, and 242,000,000 acres for 1901–1910. Making the guess—for we can make nothing better—that this area may be increased to 300,000,000 acres, and that under ordinary agriculture the average yield may eventually be increased to 20 bushels over the whole, we get an average harvest of 6,000,000,000 bushels of wheat. The average wheat eater consumes, according to Sir William Crookes's figures, about 4½ bushels per annum; but the amount tends to increase. It is as much (according to Dr. Unstead) as 6 bushels in the United Kingdom and 8 bushels in France. Let us take the British figure, and it appears that on a liberal estimate the earth may in the end be able to feed permanently 1,000,000,000 wheat eaters. "If prophecies based on population statistics are trustworthy, the crisis will be upon us before the end of this century."[1]

Interesting as such speculations are, despite the number of uncertain variables with which they necessarily deal, they fail to take into consideration the altered prospects arising out of the modern increasing knowledge of the science of nutrition. It is by no means improbable that progress in food chemistry and the study of metabolism will point the way to substitutes for what is now regarded as a staple foodstuff. We shall see what changing customs in diet have already brought about in many instances. If corn, for example, does not satisfy the requirement of a staple crop for human consumption, it is not at all unlikely, in view of information already available, that small addenda of other foods may suffice to supplement it so as to produce a more perfect ration.

One may appropriately recall here that evidences of adequate nutrition are available from people nourished in most diverse ways in different parts of the world. Even if the wheat problem were to become one of urgency within an appreciable period, this need not necessarily be construed into a forecast of an actual shortage of food. Within a few months attention has been directed to the possibility of growing in the United States at least two plant products which may serve as human foods. One of these is proso millet, the other grain sorghum or kaoliang, both of which have long been known in other parts of the world as constituents of the diet of mankind. Both of these seeds can be milled like the familiar cereals and served like these or transformed into culinary products after admixture with flour, which enables them to be prepared for baking. The peculiar agricultural advantage in such crops lies in the fact that they are drought resistant. Proso will grow when and where the staple small grains that require moist regions fail. Kaoliang represents a tropical annual plant which can by cultivation be extended north as far as Indian corn on this continent. The dietary possibilities of both proso and kaoliang have already been tested in a semipublic way.[2]

Food preservation and food conservation.—The preservation of food affects the food supply by making it possible to utilize in times and places of relative scarcity products which are available in a season and region of abundance. From an early period preservative methods have been employed. Some of them are so familiar that they are frequently not even recognized as belonging in the category of food preservation. Desiccation, canning, pickling, salting, smoking, low temperature, freezing, special chemicals—these are some of the factors that enter into this aspect of our theme. The significance of most, if not all, of these procedures is more largely economic than hygienic.

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[1] Dickson, H. N.: loc. cit. p. 555.

[2] See Hansen, N. E.: Proso and Kaoliang as Table Foods. South Dakota Agricultural Experiment Station Bull. 158, March, 1915.

The cold storage methods now in use represent a comparatively recent development of the preservation problem.

According to Sherman, only since about 1893 have the quantities of food materials placed in cold storage been large enough to have an appreciable effect upon market conditions. As an illustration of its efficiency, recent experiments have shown that fresh fish—a food product notably subject to speedy deterioration—may be preserved frozen, by the best cold storage processes, without undergoing any important change for at least two years.[1]

Modern bacteriology has placed upon cleanliness a preservative value which may appear surprising in respect to its efficiency, particularly in conjunction with low temperatures which inhibit the development of microorganisms detrimental to foods. As an example of what such sanitary precautions can accomplish in the case of readily deteriorating milk, Sherman states:

> Three American dairy farms exhibited raw milk at the Paris Exposition of 1900, one of them sending weekly shipments throughout the summer, each of which was kept on exhibition in the raw state without spoiling until the next shipment arrived. It was difficult to convince the jury of European experts of the fact that cleanliness and cold were the only preservatives needed to accomplish the keeping of raw milk in a fresh sweet condition for two to four weeks in midsummer.[2]

Precisely such methods, combined with modern transport facilities, have made it possible to extend the range of milk supply in our large cities literally hundreds of miles and to bring an indispensable food at a reasonable price into every home. There is, indeed, a profound difference between marketing milk in the familiar manner now practiced and the older mode of distribution when goats or cows were driven in front of the home to be milked there.

Probably no single preservation device excels that of desiccating the materials. In the absence of moisture decay is arrested. Where the water content of a natural food is not unduly large it can often be dried readily with success. Dried meats, fish, and fruits have long belonged to the list of preserved foods. In the case of products comparatively rich in water, particularly liquid or semiliquid foods, successful methods of desiccation have awaited the perfection which is beginning to manifest itself at the present day. Aside from the element of cost, the use of heat to expel moisture has the objection that it alters the product in some cases so that it is no longer dietetically acceptable. Heat also may remove desirable volatile ingredients. Flavors, which play a very important rôle in rendering a food acceptable to the consumer are not always thermostabile.

Modern industry is likely to overcome many of the difficulties by the device of desiccation at lower temperatures either in a vacuum or a current of air. A most satisfactory instance of this is seen in the case of milk. Condensed and evaporated milks are likely to be superseded by dried milk of which superior grades are already being manufactured. The successful desiccation of milk—a product of which seven-eighths is water—with the retention of the solubility on which the practical applications largely depend, and with its nutritive virtues presumably intact, is an up-to-date accomplishment.

The possibility of a satisfactory outcome of the efforts now being made in the milk industry deserves more than passing notice. Milk not only is a valuable food; it is at present an indispensable component of the diet during growth, and no entirely satisfactory method of preservation has hitherto been devised. With one American brand of dried milk as the chief component of the ration, several investigators, including myself, have raised small animals into a second generation. If the best dried milk

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[1] Smith, C. S.: A Study of the Influence of Cold Storage Temperatures upon the Chemical Composition and Nutritive Value of Fish. Biochemical Bulletin, 1913, iii, 54; Perlzweig, W., and Gies, W. J.: A Further Study of the Chemical Composition and Nutritive Value of Fish Subjected to Prolonged Periods of Cold Storage. Ibidem, 1913, iii, 69.

[2] Sherman, H. C.: Food Products. New York, 1914, p. 53.

of the future shall be shown to retain even the more subtle physiological properties, such as its antiscorbutic potency, it will represent good achievement.

The expression "food conservation" is used in the present discussion perhaps not in accord with a strict definition but rather in the broader current sense in which we speak of the conservation of other resources. The growing use of by-products finds its exemplification in the food industries as well as in other branches of commerce; and directly or indirectly this affects the problem of food supply. In some instances the use of the by-products has rendered the production of a food which otherwise could not be marketed advantageously profitable and therefore possible. The meat industry presumably affords instances where the price of edible parts has been kept within reasonable limits by the increasing market value of what was once merely worthless refuse. Tankage belongs to the latter category. The refinement of this aspect of modern industry impressed itself upon me in seeing the fine hairs in the ears of cattle fattening for market clipped for the special manufacture of expensive "camel's-hair" brushes; and likewise in observing the careful removal and collection of the seeds from raisins introduced into commercial mince meat. From these supposedly worthless seeds valuable raisin oil was subsequently extracted. The by-products of the sugar industries are notably important. Part of them are literally used to get gold. The residues from the desaccharification factories are rich in nitrogen which is in part converted into sodium cyanide. Tons of this have been exported to the Transvaal where it has been used for extracting the precious metal by the well known cyanide process.

For the food supply it is more important that in many instances what was in the past regarded as refuse or a useless dietary constituent has been converted into edible products. Sometimes, as in the case of grain products, in the distilleries, breweries, etc., by-products now serve as cattle feeds and thus indirectly conserves the food supply of man. In other instances new human foods have been devised. Cottonseed oil, oleo oils from beef, and other fats are no longer despised as constituents of the diet. In some cases chemistry has aided to alter the fats into a suitable texture and consistency for culinary purposes. Slaughterhouse blood finds its way into food products. Corn sirups and glucose sugars artificially prepared from cheap sources of starch have survived the propaganda of prejudice and now represent one of the cheapest sources of wholesome nutriment. Deteriorated products such as old butter are "renovated" and returned into the food treasury. Hydrogenated fats are a modern innovation.

The digestive functions of man offer a barrier to the successful use of certain agricultural products as human nutrients. Complete digestion is a prerequisite to adequate nutrition. Cellulose, which is so widely distributed in plants, is unutilized by man because it is indigestible. It is theoretically conceivable, however, that cellulose can be converted into available carbohydrate by chemical procedures. Other plant constituents, wholesome in themselves, are often practically unutilized in the alimentaty tract because they are protected by impervious coverings. In such cases the physical texture of the product is at fault. The alimentary utilization of the foodstuffs, particularly the indispensable proteins, in common foods such as the legumes and cereal grains is far below what pertains in most animal food products. Some presumably valuable vegetable proteins can not be used as food by man because his digestive juices can not get at them in the condition in which they are usually exhibited for use. Improved culinary methods and procedures for extreme comminution, particularly after desiccation, may alter this situation in coming years. A beginning has already been indicated by H. Friedenthal in the case of certain green vegetables. The growing use of nut products and nut pastes, and the widespread popularity of the readily digested peanut butter, prepared from an article which is looked upon as difficult of digestion in its imperfectly comminuted form, shows what industries can do to overcome dietary prejudices or domestic ignorance, by enhancing palatability and digestibility.

Of all the foodstuffs, the proteins offer the most serious problem. They represent the indispensable staple for tissue construction; they are produced at the greatest expense. The quantitative aspects of the protein requirement of man have been warmly debated in recent years. One extreme view of the superiority and consequent liberal need of protein was expressed by Liebig [1] as follows:

Everywhere throughout organized nature, where animal life is developed, we find the phenomena of life depending on the presence of albumen. The continuance of life is indissolubly connected with its presence in the blood; that is, in the nutrient fluid. In so far as the notions of formation, nutrition, or the nutritive property are inseparable from that of a substance whose properties and composition are collected in the word albumen, only those substances are in a strict sense nutritious articles of food which contain either albumen or a substance capable of being converted into albumen (p. 346).

The "plastic foods" of Liebig were the proteins. Accordingly he says again:

All these organized tissues, all the parts which in any way manifest force in the body, are derived from the albumen of the blood; all the albumen of the blood is derived from the plastic or sanguigenous constituents of the food, whether animal or vegetable. It is clear, therefore, that the plastic constituents of food, the ultimate source of which is the vegetable kingdom, are the conditions essential to all production or manifestation of force, to all those effects which the animal organism produces by means of its organs of sense, thought, and motion (p. 366).

The other extreme is represented by the modern so-called "low protein" advocates. From the debate on this topic it has become probable that, although some views as to the importance of protein in the dietary have been exaggerated, a liberal factor of safety must be allowed. In any event protein has lost the special significance which it assumed in Liebig's day as the unique source of energy. As a guide in the consideration of the protein supply of the future we may recall the attitude of Prof. Rubner, an expert in the field of nutrition study, before the Fifteenth International Congress on Hygiene and Demography at Washington in 1912:

Nutrition in the cities has at all times a tendency toward refinement, but in former times, when the classes lived strictly separate, the food materials were also very different within the city walls. The food of the nobility was different from that of the middle class, and the latter from that of the poor people. Among the materials successfully used in the culinary art a high place has always been held by the meat of mammals, fowls, and fishes. These meats were the chief part of the meal, other foods of vegetable origin, as salads and vegetables, sweets, and flour foods being added. Bread remained in the background. The traditions of this culinary art have remained the same down to our days. This diet of the upper classes is the only one which provides the pleasures of the table; it is rich in proteid and fat; it is not voluminous, does not overburden the stomach, tends less to obesity than any other diet, keeps the body even of a lazy man in good condition, and does not overwork the digestive functions. The less well-to-do reduce, of course, the amount of meat, but they use in its place bread and potatoes. This is called a mixed diet. When the barriers between the classes fell, the middle classes gradually rose to the more luxurious food of the formerly privileged classes.

It is a fact that the diet of the well-to-do is not in itself physiologically justified; it is not even healthy, for, on account of false notions of the strengthening effect of meat, too much meat is used by young and old and by children, and this is harmful. But this meat diet is publicly sanctioned; it is found in all hotels; it has become international and has supplanted almost everywhere the characteristic local culinary art. It has also been adopted in countries where European culinary art was unknown. Long ago the medical profession started an opposition to the exaggerated meat diet—long before the vegetarian propaganda was started. It was maintained that flour-foods, vegetables, and fruit should be eaten in place of the overlarge quantities of meat.

The descendants of those well-nourished classes are, on account of many influences, especially the school and the indoor life, not always the strongest part of the nation, but since in recent times bodily exercises have become general they are again decidedly in the ascendency.

[1] von Liebig, J. Familiar Letters on Chemistry. 3d edition. London, 1851.

The sanitary condition of the great mass of industrial workers and their children, and of people of very small earnings, are different. Here we find a decided deterioration of the body, as is amply shown by the recruiting for military purposes. In spite of continuous migration from the country to the cities, conditions are little changed. The social surroundings of a great city are decidedly unfavorable to the maintenance of a strong race. Among the many factors which cause this decrease of bodily efficiency nutrition is not the least.

The industrial workers coming from the country to the city can not well get along with their former simple diet because the cheap food materials which are easily obtained, as bread and potatoes, contain too little proteid. They undoubtedly need an increase of proteid material. Neither can they find in the city the food conditions to which they had formerly been used; but they accommodate themselves rapidly to new conditions, coming into the new surroundings, as they usually do, without a family. Just as under the doctrine of political equality the lower classes try to attain the luxurious table of the well to do, so it is not surprising that industrial workers coming from the country to the cities accommodate themselves to the new dietary forms.

The workingman does not want proteid, leguminous food, milk, etc., to improve his vegetable diet; he wants simply meat, not because he needs it, but because it is for him a matter of pride to follow as best he can the other classes in his diet. The difficulty is that the cost of meat is considerably higher than in the country where food can usually be obtained without the aid of dealers, and where many foodstuffs are raised on one's own land.

The importance of the conservation of protein has led to numerous investigations of the economy of this food stuff which need not be discussed here.[1]

Transportation facilities.—The concentration of population in restricted areas is necessarily limited by the possibilities of the food supply. The latter is the corollary of finding suitable accomodations for increasing numbers. Within less than a century nearly every region of the globe has been tapped by railways or waterway facilities to permit the more uniform distribution of things. The competition of the different lines of transportation has been an interesting phase in the exchange of commodities, among which food has been conspicuous. The end is not in sight, for with the added possibility of preserving foods at reasonable cost a new chance for distribution has arisen. American wheat has long traversed a continent by train or crossed an ocean in a steamer's hold, but the sight of Australian meats in the London market, of Californian fruits and vegetables in Boston, of eggs from China in Chicago, or of Wisconsin milk in Manila was reserved for the present generation. In earlier days the dietary habits of peoples were developed on the basis of the native products of the soil. Now, when the means of transportation are no longer primitive, specific demands can readily be satisfied by importation. This is particularly exemplified where certain habits of taste have persisted longer than the local sources of supply.

Customs in diet.—To one who has given little thought to the subject, the dietary habits of a community or nation may appear as something fairly fixed from generation to generation. This is, however, far from a correct view. Adequate nutrition may be exemplified alike among the meat and blubber eating Eskimos and the strictly vegetarian Hindoos. But particularly where the dietary instincts have led mankind to adopt a more diversified mixed ration one may discover shifts of custom and changes

[1] The following is a partial list of monographs dealing with some aspects of this topic: Chittenden, R. H.: Physiological Economy in Nutrition, 1904; Chittenden, R. H.: The Nutrition of Man, 1907; McCay, D.: The Protein Element in Nutrition, 1912; Rubner, M.: Volksernährungsfragen, 1908; Rubner, M.: Wandlungen in der Volksernährung, 1913; Hindhede, M.: Protein and Nutrition, 1913; Mendel, L. B.: Theorien des Eiweissstoffwechsels nebst einigen praktischen Konsequenzen derselben, Ergebnisse der Physiologie, 1911, xi, 418–525; Mendel, L. B.: Nutrition and Growth. Harvey Society Lectures, 1914–15.

of eating habits within comparatively short periods. A comprehensive survey of this feature of dietetics and an examination of the underlying causes would furnish interesting physiological, sociological and economic details. A few typical illustrations must suffice to indicate these interrelations between customs in diet and the food supply.

The use of fresh fruits has been enormously extended among the progressive peoples of temperate zones within the past two decades. Some of these food products, such as orchard fruits, have long been favorites in the dietary and because of their superior keeping qualities have been available over long periods of the year. The output of orchard fruits has kept pace with the growth of population. The value of the products of the orchard in the United States in 1840 was about $8,000,000; a recent census report gives the figure as $140,867,000. Among other types of fruits proportionately greater increases are noted. "Small fruits" contributed $30,000,000; grapes, $22,000,000; citrus fruits, $23,000,000; other tropical and subtropical fruits, $2,000,000; to the production of fruits in the United States in 1909. Many of these, like the orange and grapefruit, have become prominent in the diet of the well to do because of the readiness with which they can be obtained at a reasonable price everywhere during most of the year. Science, the mechanic arts, and business organization have combined to revolutionize the distribution and marketing, as one may learn in studying the work of the California Fruit-Growers' Exchange. The once enormous losses from decay have been greatly reduced and the marketed products are of a superior quality.

There is a physiological justification for the increasing prominence of fruits in the diet of the better classes and its extension throughout all seasons of the year. With the growing use of highly digestible foods and the exclusion of indigestible food residues, with the widespread employment of milled cereals largely freed from cortical parts, with the tendency to exclude the "coarser" vegetables or limit their inclusion in the menus of the better classes, the absence of "roughage" in the diet, combined with other features of modern living, helps to induce habitual constipation in certain classes of society. The fruits serve a useful purpose in counteracting this tendency by promoting the movement of the bowel—hence the expression, "An apple a day keeps the doctor away."

The familiar adage just quoted has been converted into an advertising slogan in some of the apple-growing States of the West. This leads me to call attention to the potent force of advertising in creating a demand for food products of most varied sorts. The same agency which has created a nation-wide mania for chewing gum and has initiated in all ranks of society a senseless habit of mastication which was until a few years ago limited to the overlooked improprieties of childhood, has been reflected in the food market. The ready-to-eat "breakfast foods" in highly advertised, neat, and attractive packages, have replaced the less expensive cereals long sold in bulk. The change is not merely one of the container or package; the contents no longer are the same. Oatmeal, for example, has lost some of its former popularity as a breakfast dish with the inroad of corn flakes and wheat foods. The breakfast staples have been changed by the modern advertiser; and illustrations of his ingenuity might be extended to include numerous food products. Except from the standpoint of extreme economy the innovations have as a rule been wholesome and usually in the interest of food hygiene. The purity of the products has not infrequently surpassed the honesty of the advertisement.

Most of us can recall the days when meat or eggs, or both, formed an indispensable part of the early meal in the United States. At present there are signs everywhere, at least among those classes which are not engaged in more vigorous muscular work, of a simplification of this meal by the exclusion of meat and the substitution of cereals and fruits. This is an approach to the traditional breakfast of continental Europe.

It is not easy to analyze the underlying causes for such dietary changes; they are not solely physiological nor economic in origin. Rubner has remarked that sometimes revolutions occur in the field of popular nutrition. The introduction of the potato in many extensive regions is cited as an illustration.

It might be supposed that bread, "the staff of life," remains essentially what it has been in days gone by. This food product, however, furnishes an example of the evolution of a food industry. Bread making is gradually becoming a factory problem. The magnitude of this may be appreciated from the statement that the baking industry is to-day capitalized at over $270,000,000; yet housekeepers still make 70 per cent of the product used.[1] With increasing efficiency and range of distribution the use of bakers' bread is certain to increase; just as butter, pickles, mustard, etc., are no longer exclusively home-made products. As soon as larger corporate interests become involved in the food industries, altered methods of manufacture are likely to be introduced when they seem both profitable and feasible. Food innovations are not readily introduced in the home, but in the factory they frequently become questions of dollars and cents. In the manufacture of baked goods the cost of production has been modified by the substitution of dried milks for fresh milk and of vegetable fats for the more expensive butter. The manufacture of yeast has become specialized into an important industry which reacts upon the public with the cleverly advertised admonition to "eat more bread."

Wheat has unique properties which adapt it to the production of bread as we now know it. Other seeds are competing for recognition. New "flours" are proposed. The proso and kaoliang flours already mentioned are among them. Even cottonseed "flour" is clamoring for recognition. When glutenous adjuvants are supplied to cereals which lack them, and when more science is infused into the art of baking, new bakery products are likely to arise.

The use of fats in the diet is doubtless increasing in the United States. It is estimated that the consumption of butter alone reaches 23 to 24 grams (three-fourths to four-fifths of an ounce), or approximately 200 calories per person per day. An inspection of the dietaries in the public establishments of half a century ago, as they are reported in the treatises of that period,[2] reveals the important part taken by bread in the regimen. Butter was often entirely omitted in the daily allowances of asylums, prisons, military groups, and other typical institutions. Frequently the diet lists of those days call for bread and molasses or bread and milk. Bread without butter or some other fat is now the rarity, at any rate in American homes. Despite the discouragement which the oleomargarine industry has received from legislation, ofttimes unwarranted, the use of butter substitutes is spreading as the price of the original product is increasing. Here too the advertising billboards are already pointing out the future way. Butter substitutes are not only used directly in the meal, but are finding a wide field of application in the cooking and baking processes of the kitchen.

Another change in diet customs is seen in the growing use of cheese in American homes. This wholesome article has long been appreciated at higher value in European countries than in our own. Nuts and nut foods are becoming more popular, in part as the result of the modern vegetarian propaganda which recommends them as "meat substitutes." The value of the peanut crop is about $20,000,000. Sherman remarks that "to speak of nuts as 'meat substitute' is natural under present conditions and reflects the prominence which has been given to meat and the casual way in which nuts have been regarded for some generations. Looking at the matter in evolutionary perspective, it might be more logical to speak of meats as 'nut substitute' instead."

[1] These statistics and related statements are taken from Duncan, R. K.: Some Chemical Problems of To-day. Chapter on Bread.

[2] For example, in Pereira, J.: A Treatise on Food and Diet. New York, 1843.

The current extensive use of sucrose in the form of refined cane sugar or beet sugar exemplifies what the cheapening of an article of commerce can accomplish in the field of diet. Although sucrose has a considerable fuel value in the organism its dietary use is primarily dictated by considerations of flavor. Opinions are occasionally divided as to the place of this sugar in the dietary. It seems as if the extremes of refinement which have made commercial sucrose in a chemical sense the purest of all purchasable foodstuffs had exceeded all requirements of nutrition or dictates of the palate. The addition of a blue dyestuff to give a white appearance to the final product represents one of the psychological values which are often more ridiculous than costly. Surely for most uses the artificially colored white sugar has nothing except a false standard to recommend it in place of the natural cream colored sugar.

It is likely that the succulent vegetables will play a larger part in the table of American households. Dr. C. F. Langworthy, Chief of Nutrition Investigations in the Office of Experiment Stations at Washington, says:

One of the marked differences between the daily fare to-day and that of 50 years ago consists in the increased supply of green and succulent vegetables, a class of food used, as their names imply, for their refreshing and palatable qualities more than for their total nutritive value. Not many years ago the winter's supply of vegetables in all southern countries was limited to root crops and a few other staples, such as onions and cabbage, which could be kept in the cellar in comparatively good condition. New and improved varieties, better methods of cultivation, improvements in transportation and storage, the great development of market gardening under glass, and the development of the canning and preserving industry, have made succulent vegetables common throughout the year and available in one form or another for almost every family.[1]

The popularity of green vegetables is beginning to be reflected in the canning industries where the variety of such products is being extended rapidly and the canning process has already developed into an important enterprise. To the more familiar commercial lists including tomatoes, corn, peas, and beans, there are being added asparagus, beets, okra, pumpkin, sweet potato, rhubarb, sauerkraut, spinach, and squash. The extent of this canning industry and its growth in a single decade is shown statistically, as follows:

Extent of the canning industry in the United States.[2]*—Quantity and value of foods canned, 1899 and 1909.*

	1909		1899	
	Cases.	Value.	Cases.	Value.
Vegetables	32,752,469	$51,568,914	19,323,730	$28,734,598
Tomatoes	12,909,986	18,747,941	8,700,538	13,666,560
Corn	7,451,265	10,332,136	6,336,984	8,191,383
Peas	5,901,703	10,247,363	2,543,722	4,465,673
Beans	3,392,864	6,013,098	1,493,517	2,025,123
Asparagus	228,559	1,975,775	----	----
Pumpkin	440,303	576,043	138,078	202,404
Sweet potatoes	347,286	631,651	83,526	124,245
All others	2,080,503	3,144,907	27,365	59,210
Fruits	5,518,999	12,938,474	4,467,817	11,311,062
Peaches	1,484,808	3,753,698	1,449,356	4,283,165
Apples	1,205,742	1,898,720	645,762	1,125,119
Apricots	630,185	1,825,311	531,648	1,538,252
Pears	637,782	1,833,214	672,485	2,188,201
Berries	815,851	1,754,927	600,419	1,092,975
Cherries	390,351	1,019,013	114,367	307,788
All others	354,280	853,591	453,780	730,562

[1] Langworthy, C. F.: Green Vegetables and Their Uses in the Diet. American Food Journal, Oct. 15, 1912, p. 5.

[2] From Bitting, A. W.: Methods Followed in the Commercial Canning of Foods. U. S. Department of Agriculture, Bulletin 196, Washington, 1915.

The indirect effects of the antialcohol campaign now vigorously conducted in many countries are seen in the stimulation of trade in so-called temperance drinks. It comes as a surprise to an old-timer to see buttermilk retailed over the bar of the American saloon. The grape-juice industry has grown by leaps and bounds; and this alcohol-free natural product is veritably becoming one of the national drinks. I am informed from expert sources that the production of American unfermented grape juice in the year 1914 amounted to 4,593,750 gallons in the Chautauqua belt alone. Other fruits, also, are likely to figure in the new field of use here opened. It is stated that 25 per cent of the apples grown in American orchards never enter into the food supply of the nation. This has been a stimulus to the food conservationists to transform the unused materials into new forms of food. Apple sirup and concentrated cider have been suggested as new products for utilizing surplus and cull apples.[1] The expert of the Department of Agriculture remarks:

What the commercial future of the two products will be remains to be determined under actual marketing conditions. The department has every confidence in the feasibility of making the two products where the apple supply and the manufacturing conditions are suitable. The development of this infant industry must now be left in the hands of the progressive American manufacturer. A process which will make pure, fresh cider available as a summer drink at our soda fountains should open up a new and valuable market for the juice of surplus apples. Whether young America will eat apple sirup on his bread and his mother use it in her kitchen must be decided by the American people.

Similar considerations are being applied to other fruits now wasted.

The "dairy lunch" rooms of our cities and larger villages represent an innovation in dietary practice. The dinner pail and the lunch basket filled with homemade food have given way to "ready-made" meals. To one group of persons the lunch rooms represent a welcomed escape from the more expensive luxuries of the conventional restaurant; likewise a possibility of substituting old-fashioned pastry and cereal dishes for the usual dining-room meal rich in meat. To another increasing class, however, they offer a means of reducing the labor of the household by the device of a public eating place. The recent interesting study of a familiar chain of these "dairy" restaurants, published under the auspices of the Sage Institute by Gephart and Lusk,[2] show that the popular sandwich meal of the lunch counters is by no means a cheap diet for the working classes who have a limited allowance to spend for food. Attractive as the highly profitable service of the "dairy lunch" may be, with its congenial environmental features, it can not compete with "home cooking" from the standpoint of economy. This lesson needs to be brought home to a nation which is continually discussing the high cost of living. Domestic arts should not become relegated entirely to corporate enterprise.

Changing social and industrial conditions and other economic and hygienic factors.— Rubner has pointed out an interesting effect of commerce in food on nutrition:

Most conservative as to the food question, is the farmer, though in the country, too, many changes are taking place. He has frequent contact with the city, but he has still plenty of food material, though not always quite suitable to the purpose. I have noticed a very unfavorable influence of urban food requirements on the milk-producing districts of some regions of Switzerland and Germany, which is so characteristic that it deserves consideration. The milk-producing regions of the Bavarian highlands and of Switzerland had formerly an extremely healthy, strong, and temperate population. Milk was largely used as a food, and the excess of production was placed on the market. In the course of years the communities gradually established central diaries in which the fat is withdrawn from the milk by means of centrifugal machines to produce cream and butter. The impoverished milk is partly

[1] See Gore, H. C.: Apple Sirup and Concentrated Cider: New Products for Utilizing Surplus and Cull Apples. Yearbook of the Department of Agriculture for 1914, Washington, 1915, p. 227.

[2] Gephart, F. C., and Lusk, G.: Analysis and Cost of Ready-to-Serve Foods. Press of the American Medical Association, Chicago, 1915.

returned to the farmers. The milk producers are paid in cash for their product, but a poor and insufficient food takes now the place of a former healthy one. The money now goes to the saloons. The potato conquers a new territory. Instead of the butter which was formerly used, cheap fats are now bought; in short, the change of diet is exactly such as we find with the poorer working population in the cities. The effects are exactly the same. Physical deterioration in such districts becomes more and more pronounced, reaching finally a low level. This is a very serious condition, which attracts attention and which must be combated by all possible means.

Rubner believes, further, that the industrialization of nations is attended by a change in body weight, not because the race has changed in itself, but because the nutritive conditions have changed for a large number of laboring people through migration to the cities. To-day only a small proportion of the industrial establishments are in rural communities, where the living conditions are favorable. The problem of the underfed is thus closely related to the distribution of the food supply.

The present European war is affording an opportunity to study the relation of the food supply to unexpected economic and territorial conditions. From the standpoint of Germany the situation is unique in view of the exclusion of food normally obtained in large amounts from abroad. Russia, America, and other countries have hitherto furnished wheat, rice, butter, lard, eggs, and many other foods, along with cruder feeds, which in turn were applied to animal production. These sources have been threatened or entirely cut off. With true scientific acumen the German nation has started a public propaganda of advice intended to meet the situation thus unexpectedly created.[1] The export of native products, such as sugar and rye, is to be restricted; the feeding of materials suitable for human consumption to cattle is to be greatly decreased and conservation of food values ordinarily lost in the processes of conversion into animal tissue accomplished; unjustifiable waste is to be avoided not only in the trade at large, but in the individual kitchen. The elaborateness of the investigation is indicated by such details as the reminders that 20 grams of fat per capita are lost in the sewage waste of Berlin every day, and that this ought to be prevented. The people are assured, on the authority of eminent scientists, that they need not fear intelligently instituted changes of dietary régime as something inimical to health.

The laws of nutrition and suitable dietetic advice are being proclaimed and distributed in popular form.[2] The more liberal use of plant products (rich in carbohydrates) in place of meats (rich in proteins and fats) is urged. As a move in the direction of economy in nutrition the gradual substitution of the regimen of south German households in place of the excessive meat diet of the northern provinces is urged. Even a cookbook for war times is freely supplied.[3]

The experience of the commissary department of the United States Army in Cuba during the campaign of 1898 has taught the mistakes not only of disregarding local conditions, but also of failing to grasp important dietary principles and to inculcate them where the lessons are needed.

No presentation of the problems of the food supply would be complete without an appreciation of what the growing science of physiology and the chemistry of foods is contributing to mankind. The calorie idea in nutrition, the outcome of an understanding of the transformation of energy in the living body, has been fruitful in more ways than one. It has taught people to think of the uses of food from a more rational standpoint and has furnished an intelligible basis for constructive institutional dietetics, as well as the nutrition of the individual. Food is beginning to be regarded

[1] See Eltzbacher, P.: Die Deutsche Volksernährung und der Englische Aushungerungsplan. Fr. Vieweg & Sohn, Braunschweig, 1915.

[2] For example, in pamphlets such as "Ernährung in der Kriegszeit," ein Ratgeber von Prof. Dr. Paul Eltzbacher, Frau Hedwig Heyl, Prof. Dr. Carl Oppenheimer, Prof. Dr. Max Rubner und Prof. Dr. Nathan Zuntz. Braunschweig, 1915, pp. 16.

[3] For example, the "Kriegskochbuch," von Frau Hedwig Heyl. Berlin, 1915.

as fuel for the human organism—something that must be provided in determinable amounts. Malnutrition and undernutrition have received a new popular significance in the discussion of human efficiency.

This is not the place to discuss the limitations of the calorie idea in nutrition or of some of the current conceptions of the rôle of the individual nutrients—the proteins, fats, carbohydrates, and inorganic salts. There is a well-founded growing belief that an important part in nutrition is played by substances which are not identical with the familiar foodstuffs mentioned and which, despite the minimal amounts thereof present in the diet, may nevertheless be indispensable for growth and the maintenance of life. They have been called "accessory diet factors" or "vitamins." We may conceive of them as stimulating certain physiological processes and as essential to certain functions.

The lubricant is quite as important to a machine as is the energy-furnishing fuel. So these diet accessories may have a peculiar usefulness. They are apparently sometimes easily impaired by heat; in the language of the chemist, they may be thermolabile. Hence the use of heat for preserving or sterilizing foods suggests new difficulties. They may sometimes be lost in the wastes of the modern technical processes, as in the milling of cereals. This has been demonstrated in the case of "polished" rice. They may be sensitive to other agencies involved in the change from fresh to salted or "prepared" or preserved foods.

These topics represent the border line of our knowledge of to-day. Enough facts are known, however, to justify the interest which the subject is receiving. Scurvy has long been recognized as a disease related to diet and the antiscorbutic and curative virtues of certain food products like lemon juice were early learned by experience. To these so-called "deficiency diseases," beriberi and possibly pellagra, rickets, and Barlow's disease may be added. I have discussed special features of this question elsewhere.[1] They help to explain the occasional failure of one-sided dietaries, and possibly the incidence of disease in groups of people living through ignorance under restricted conditions of diet, in institutions, on expeditions, on shipboard, during famine, and sometimes amid plenty.

The danger, if there be such, of a lack of unrecognized diet accessories is probably greatest in the exclusive use of "artificial" foods which have experienced extensive alterations in the course of their commercial preparation. In the present stage of our knowledge variety of food, including fresh foods of many descriptions, may be welcomed on this ground alone. Canned goods, glucose, margarine, refined sugar, highly milled cereals—in themselves skillfully produced specimens of modern technical progress—should be supplemented with fresh foods for safety until our knowledge has grown to supersede the uncertainty of present-day ignorance about unappreciated deficiencies of the diet. If the factory and organized business have introduced "artificial" products, modern industrial organization and transportation have likewise increased the possibilities of physiological liberality in diet. The studies of the past few years on the physiology and chemistry of the ripening of fruits is only one indication of how science is enlarging the possibilities of the food supply through an understanding of underlying factors. Useful investigations on the date, the banana, the apple, and other fruits have already been instituted by our Government.

The recent progress in the physiological chemistry of the proteins illustrates a trend that is likely to affect feeding practices in the future. The protein molecule is composed of a group of unlike chemical units many of which appear to be indispensable for the nutritive functions. The animal body can not construct all of these synthetically, hence it is dependent upon a supply thereof in the diet. The proteins of common foods furnish unlike yields of these essential units or tissue "building stones."

[1] Mendel, L. B.: Nutrition and Growth. The Harvey Society Lectures, 1914-15. Also Journal of the American Medical Association, May 8, 1915, p. 1539. The literature of the subject is presented there in some detail.

It is accordingly becoming apparent that a well-selected ration must furnish these in both quantitative and qualitative sufficiency. Corn and the by-products of the maize kernel are notably inadequate for good feeding results unless they are supplemented by other protein-containing foods. The relative economy of the addition of supplementary proteins, such as are present in dried blood or milk products, to a ration that is inexpensive, but inefficient by itself, suggest new standards in our feeding practices. A small addition of an adequate protein may be far more advantageous for producing gains in animal husbandry than large amounts of cheaper proteins which supplement the deficiency of the basal ration less well.[1] Our agricultural experiment stations are becoming alive to the opportunities here opened. Fodder analysis has taken a new turn.[2] It is probable that protein feeding in the future will be based on the known chemical structure of the feeds quite as much as on the results of past feeding experiments. Here, as so often before, the investigations of what is sometimes contemptuously referred to as "pure" science have furnished results of great importance to practical nutrition. Sir William Crookes, whose frecast of the failing wheat supply has been referred to, could scarcely foresee that the progress of physiological chemistry might in itself nullify the contentions which he vigorously defended.

A corollary of a better understanding of the principles involved in the field of human nutrition is the improvement of household science and the domestic arts. Herein lies the significance of the notable "home economics movement" of the present time. Nutrition and its relation to the food supply are in no small measure a problem of the home. Just as the lessons of modern science are permeating the practices of up-to-date agriculture, so they ought to influence and modify the performance of the household. The latter has been described as a social institution employing certain material agencies which include the provision of food and clothing. Its relations to other social institutions are manifold. Upon industry, for example, the household exerts an influence by maintaining the physical vigor and efficiency of the worker; and industry, in turn, affects the home by the character of the supplies which it furnishes. We are told that the household is the ultimate agency in the distribution of economic wealth to individuals.[3] What the wage earner really secures and the wife and children secure depends upon the efficiency with which the household turns the wage income into economic good and, at the same time, supplements it by the income equivalent of household work. The contribution of productive housework is too little emphasized. The home can become responsible for malnutrition and insanitary living. An appreciation of food costs, of efficient marketing, of the "casual sequence of food from the farm to the dining room," of the preparation of food for the table, surely is of fundamental import in every home. The culinary art, upon which so much may depend, is in danger of deteriorating in the homes of this country. The admonition to "cook at home" should be passed on to the less well-to-do classes and the education of their young in the applications of domestic science should be warmly defended. No baker's bread equals the best home-made product. Too few women of the working classes are equipped to meet the demands which the home should properly make upon them.

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[1] Cf. Osborne, T. B., and Mendel, L. B.: Feeding Experiments Relating to the Nutritive Value of the Proteins of Maize. Journal of Biological Chemistry, 1913, xiv, 31; American Journal of Physiology, 1913, (a), xxxi, 16; Nutritive Properties of Proteins of the Maize Kernel. Journal of Biological Chemistry, 1914, (b), xviii, 1. Osborne, T. B.: The Nutritive Value of the Proteins of Maize. Science, 1913, xxxvii, 185. Osborne, T. B., and Mendel, L. B.: The Comparative Nutritive Value of Certain Proteins in Growth, and the Problem of the Protein Minimum. Journal of Biological Chemistry, 1915, xx, 351; Protein Minima for Maintenance. Ibid, 1915, xxii, 241.

[2] Cf. Nollau, E. H.: The Amino-acid Content of Certain Commercial Feeding Stuffs and Other Sources of Protein. Journal of Biological Chemistry, 1915, xxi, 611; Grindley, H. S., Joseph, W. E., and Slater, M. E.: The Quantitative Determination of the Amino-acids of Feedingstuffs by the Van Slyke Method. Journal of the American Chemical Society, 1915, xxxvii, 1778.

[3] Cf. Andrews, B. R.: A Course in Household Economics. Journal of Home Economics, February, 1913, p. 26.

Many years ago Liebig wrote, in his Familiar Letters on Chemistry:

Among all the arts known to man there is none which enjoys a juster appreciation and the products of which are more universally admired than that which is concerned in the preparation of our food. Led by an instinct, which has almost reached the dignity of conscious knowledge, as the unerring guide, and by the sense of taste, which protects the health, the experienced cook, with respect to the choice, the admixture, and the preparation of food, has made acquisitions surpassing all that chemical and physiological science have done in regard to the doctrine or theory of nutrition. In soup and meat sauces he imitates the gastric juice; and by the cheese which closes the banquet he assists the action of the dissolved epithelium of the stomach. The table, supplied with dishes, appears to the observer like a machine, the parts of which are harmoniously fitted together and so arranged that, when brought into action, a maximum of effect may be obtained by means of them. The able culinary artist accompanies the sanguigenous matter with those which promote the process of solution and sanguification in due proportion; he avoids all kinds of unnecessary stimuli, such as do not act in restoring the equilibrium; and he provides the due nourishment for the child, as well as the old man, as well as for both sexes.

Even Liebig, the great scientist, could not adequately visualize the application of science in the kitchen. Man no longer depends upon his instincts alone for guidance in the affairs of life; otherwise progress would indeed be slow. Instruction in domestic science ought to become a means of solving the problems of applied nutrition; and the best interests of the home—economic as well as social—call for better domestic service, a discipline into which woman will enter "mit Lust und Liebe."

We have seen that the problem of food supply is not one which can be dismissed by the social philosopher or solved by the calculations of the economist. It is highly complex with its involvement of factors and interests in agriculture, commerce, industry, and nutrition. Here, as in other domains, there is opportunity for an interplay of science and the arts, of experience and investigation. To attempt to foretell the future seems more like an act of ill-considered rashness than a keen intellectual venture. The truth can only be approached scientifically. We are beginning to learn what real food values mean. There is as yet no ideal ration. The world menu is not in sight. Fitting, indeed, on this occasion are the words of Prof. Rubner:

The nutrition of the great mass of the people is a question of the highest importance, deserving far more attention than it has hitherto received. All the great countries ought to have a central authority, a food commission, which should concern itself exclusively with the far-reaching questions of the well-being of the people. The material as it lies before us to-day is very incomplete but suffices to indicate the main lines of useful work. The nutrition of the masses has so far been mostly studied with regard to political economy and according to methods and viewpoints which do not always withstand the tests of the physiology of nutrition. Only by means of the physiology of nutrition is it possible to carry on exact research.

The nutrition of the masses is to us a problem which may be approached and improved from many sides. It is necessary that not only the hygienists in the narrower sense take up the struggle for betterment but that also the great army of men, who are truly humane in their hearts, shall take their places beside us. The battle which we have to carry on is not only against unavoidable and natural difficulties; we must not forget that human society includes many elements, unwilling to make the least concession to a humanitarian movement, persons whose prosperity is selfishly held superior to the welfare of their neighbors and who will oppose such a movement with all the means at their command. Let us hope that our opponents will, at the last, rejoice with us in a triumph of the Humane Idea. [1]

[1] Rubner, M.: The Nutrition of the People. Journal of Home Economics, 1913, v. 1.

A SAFE AND SANE MILK SUPPLY.

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There are three large phases to the milk problem which may be summed up in three words—dollars, dirt, and disease. The three phases must all be solved before we have solved the milk question. Nor is one of these phases more important than another for milk which does not pay for itself will not long be produced, dirty milk will not be used when the people are informed, and milk which carries disease will eventually be barred from sale. It is the purpose of this paper to consider these three phases separately and collectively in order to discover, if possible, a sane solution of this perplexing question.

THE FINANCIAL ASPECT.

Until quite recently milk was produced under primitive conditions at a moderate cost which was roughly proportional to its food value. Although the food value has not changed materially the cost has increased decidedly, due largely to the increased cost of production. A certain part of this increase is due to economic conditions over which the dairyman has no control; another part, and this is probably the larger, is due to the changed methods of handling the product. Formerly, cheap barns, simple vessels, and common labor sufficed; now certified milk is produced in costly stables under a sanitary elegance which rivals that in our homes, with apparatus that is elaborate and expensive under expert supervision which is required for its care and management. The increase in price from 5 cents a quart to 10 cents, then 15 cents, and sometimes to 20 cents became necessary, and even now certified milk is not generally profitable. It is quite obvious that certified milk is essentially a luxury beyond the means of the vast majority of our population, and can only be indulged in by the wealthy. Evidently certified milk as a solution of the milk problem is doomed to failure. It is probably unnecessary to state what is meant by certified milk, for it has been adequately described in many sources.[1] The ideal of certified milk has been of inestimable value in an educational way for it has taught us many things. It has taught us what clean milk means and how dirt can be eliminated; that bacteriologically clean milk is essential; and that disease germs in milk can and must be eliminated. To accomplish this task has been eminently worth while, and we shall always value this service, but it is certain that simpler means must be found to accomplish the ends sought. Fortunately the work of Harding [2] and of North [3] has shown that this can be accomplished and that milk of an excellent quality can be produced without elaborate equipment and at reasonable cost. Intelligent care and a modest bonus for a superior product are the essentials for accomplishing the end in view. Before discussing this further it is desirable to consider the question of diseases carried by milk.

THE PROBLEM OF DISEASE.

That milk is a carrier of disease germs is now common konwledge and many well authenticated epidemics testify loudly to the fact. The problem of how to make milk safe as food has been attacked in a number of ways; all, however, fall under two principles, viz, either prevent the entrance of disease bacteria to the milk or kill the disease bacteria which may happen to enter. Of these two principles the former is plainly the ideal, and acting on this plan inspected milk and certified milk have been produced. Doubtless dairy inspection and milk certification have done much to lessen milk-borne disease, but it is quite obvious that inspection will not detect all diseased

[1] Bull. 56. Milk and its Relation to the Public Health. U. S. Pub. Health & Marine Hospital Service.
[2] Harding, Ruehle, Wilson and Smith: The Effect of Certain Dairy Operations upon the Germ Content of Milk.
[3] North: The Dairyman v. The Dairy. Am. Jour. Pub. Health, v. 6, 519, 1915.

animals or attendants or discover and close all the avenues by which disease organisms may enter the milk supply. The epidemic of sore throat which occurred near Boston [1] was carried by one of the superior dairies, and doubtless disease germs find their way into certified milk more often than we are wont to believe. The American ideal of certified milk fails mainly, however, because it results in too expensive a product for common use..

In Europe the tendency has been to follow the second principle, viz, to kill the disease bacteria which may enter the milk supply. This was done empirically for centuries by simply boiling the milk at home; more recently pasteurization has been resorted to, and this method is rapidly gaining favor in America as well. The greatest objection to these methods is the cooked flavor imparted to the product, but even this is largely overcome under present methods of pasteurization, and apparently we are slowly outgrowing our prejudices against pasteurized milk. While pasteurization adds somewhat to the expense, this factor is balanced by the saving affected in added keeping qualities of the product. If the pasteurizing has been properly done, we may assume that the problem of disease carried by milk is solved, for as Rosenau [2] points out, "there is not a single instance on record in which a milk-borne outbreak [of disease] is recorded from the use of pasteurized milk." While this solution may not be the most ideal one it is a practical solution which we may accept for the present as the best available and on the whole as quite satisfactory. If an occasional consumer objects to pasteurized milk, the certified product would still be available.

Many sanitarians have objected to the conclusion at which we have arrived on the ground that pasteurization is practiced on milk frequently highly polluted by manure; they have rightly held that while pasteurization rendered such milk safe, it did not change its filthiness and unfitness for human food. This contention must be granted, and this brings us to the third aspect of the milk problem.

THE PROBLEM OF ELIMINATING FILTH.

At the present time the task of eliminating dirt from milk presents the most serious difficulties, and is the most important phase of present sanitary endeavors. This problem resolves itself into two distinct phases: First, the problem of finding the most suitable method of detecting dirt in milk; secondly, bringing the evidence home to the dairyman and making him respond to the new demands. Let us first consider the methods of detecting filth in milk.

Three methods are in use more or less commonly, viz: (1) Determining the total number of bacteria present in the milk, assuming this to be an index of its cleanliness, and fixing a limit beyond which the count may not go, otherwise sale is forbidden; (2) determining the number of B. coli present and setting a similar standard; (3) determining visible dirt, and again making a standard for purity. To these the writer now desires to add another: (4) Determining B. sporogenes and creating a standard of purity.

It is well known that the total count depends upon other factors as well as upon dirt, for time and temperature may cause a high count in an otherwise clean milk; doubtless such milk should be barred from sale, but it does not reach the real question, which is the amount of dirt present in it. Again, if the milk is pasteurized, the total count fails utterly to indicate dirt. Since the use of pasteurized milk is rapidly increasing, the ultimate failure of the total count is obvious.

As to determining the number of B. coli and using the data to indicate manure, this method will fail for the same reasons that the total count must fail. In addition, the determination of B. coli requires rather too elaborate a technique to make it generally available. Up to the present time the method appears to have gained little favor.

[1] Winslow: An Outbreak of Tonsillitis or Septic Sore Throat in Eastern Massachusetts and its Relation to an Infected Milk Supply, Jour. Inf. Dis., X, 1, 72, 1912.

[2] Rosenau: The Milk Question, 1912.

When the test is made sufficiently early and before the milk is pasteurized it has been shown [1] that the method is an excellent one for the purpose. The dairy in which the method was applied received its supply from a comparatively limited area and from only 20 dairymen. Special endeavors were made to produce only superior milk.

At present the determination of visible dirt appears to be in greatest favor and has proved itself a valuable asset to the sanitarian in checking up supplies. The ease with which the determination is made and the telltale nature of the evidence presented speak highly in its favor. The Wizzard Sediment Tester [2] has proved very satisfactory in our hands. Indeed, the method leaves little to be desired so long as the producer does not become wise and adopt clarification methods such as heavier strainers or centrifugation. Obviously the method will fail as soon as better clarification methods are adopted. Such clarification can not lessen the number of manure bacteria in milk or the soluble portion of the manure, but rather aids in their better distribution. From these considerations it is quite clear that we have no method for determining manural pollution which does not fail at some critical point, the total count, and B. coli determinations fail in milk that has been held for some time or has been pasteurized, and the sediment test fails after clarification.

To overcome these difficulties is the purpose of the B. sporogenes determination as an indicator of manural pollution as proposed by Weinzirl and Veldee.[3] B. sporogenes is an intestinal organism, and hence indicates manure when found in milk; it does not multiply at ordinary temperatures at which milk is held, and so it truly indicates the pollution even of milks kept for varying periods of time and at varying temperatures; it produces spores but these are not killed by pasteurization and, finally, the organism can be easily and quickly determined.

The method for determining B. sporogenes, as we now use it, is as follows: Milk is dispensed in ordinary test tubes and solid paraffin sufficient to make one-eighth inch layer is then added and the whole sterilized. Five cc. of milk are added and the tubes heated to 80° C. for 10 minutes. The tubes are rapidly cooled, the paraffin hardens and produces an anærobic culture in which the B. sporogenes grows when incubated at 37° C. for 48 hours. The gas produced by the fermentation of the lactose lifts the paraffin plug some distance, and this is taken to indicate B. sporogenes as present.

Thus far we have not attempted to establish a standard of purity or limit beyond which the presence of B. sporogenes would condemn the milk and doubtless the line to be drawn will vary for different localities. In 1,088 samples from 20 producers analyzed by Weinzirl and Felder [1] it would appear that the presence of B. sporogenes in 5 cc. samples of milk would condemn about 20 per cent of the milk under comparatively favorable conditions. Perhaps 2 or 3 positives out of 5 samples of 5 cc. each would give a fairer standard and a broader basis for judging the purity of the milk. The above analyses have shown, however, that B. sporogenes compares very favorably with B. coli as an indicator of manural pollution when visible dirt is taken as a standard, and both are superior to the total bacterial count when the latter is made from agar plates incubated 48 hours at 37° C.

THE MILK PROBLEM AS A WHOLE.

While we may dissect the milk problem and examine each part separately, to really solve it we must consider it as a whole. We have made excellent progress, but this has scarcely been proportional to the work done, due largely to the failure to see the problem in its entirety.

We must have cheap milk, clean milk, and safe milk. Of these three purposes, the last, safe milk, may fairly be regarded as solved; the consumer has the choice of two

[1] Weinzirl, John, and Felder, H. A.: Unpublished data.
[2] Wizard Sediment Tester: The Creamery Package Mfg. Co., Chicago, Ill.
[3] Weinzirl and Veldee: Am. Jour. of Pub. Health, 5:9:862:1915.

possibilities, either pasteurized milk or, if his purse permits the indulgence, certified milk. As to cheap milk, this problem will solve itself when the dairyman is not compelled to install expensive equipment; when care is made superior to barns and machinery; when demonstration will supersede the score card. If the score card is retained at all, the resulting product must receive at least nine-tenths of the score, while the equipment and method should receive perhaps one-tenth of the credit. It is doubtful, however, whether the score card should be retained. A rating based upon the available laboratory tests would appear to be the better plan. Grading the milk on the basis of such laboratory tests into A, B, and C grades, and requiring these grades to be placed on the bottles or containers, will come nearer to solving the cleanliness problem than the clumsy and costly methods now in vogue.

SUMMARY.

To sum up the problem of a safe and sane milk supply, we find:

(1) That pasteurized milk, when the process has been properly carried out, is safe so far as disease is concerned; certified milk is also satisfactory in this respect.

(2) That a sane milk supply must be free from excessive dirt. To eliminate dirt, the milk should be rated on the basis of laboratory tests, such as: (*a*) Total count; (*b*) B. coli determination; (*c*) visible dirt test; (*d*) B. sporogenes determination.

The milk should be graded according to the laboratory tests in A, B, and C grades, and these placed upon bottles and containers in which the milk is sold.

(3) That a sane milk supply must be cheap enough to be within reach of the common people. For this purpose certified milk is a failure; on the contrary, if dairy demonstration supersedes dairy inspection, and laboratory tests the score card in grading milk, when care is made superior to equipment in barns and machinery, then a clean milk may be had at a reasonable price as well.

PROYECTO DE ORDENANZA REGLAMENTARIA DEL COMERCIO DE LECHE DE CONSUMO DE BUENOS AIRES, ARGENTINA.

Por RICARDO SARMIENTO LASPIUR,

Secretario de la Asistencia Pública de Buenos Aires, Argentina.

CAPÍTULO I.—CONDICIONES DE LA LECHE.

ARTÍCULO 1. La leche destinada al consumo debe ser la mezcla perfecta del producto del ordeño completo de por lo menos cuatro vacas sanas, bien mantenidas y cuidadas y que no se hallen en los días inmediatamente anteriores ni en los primeros días posteriores a la parición, obtenido y tratado en condiciones higiénicas hasta el momento de su consumo y sin agregados ni sustracciones ni alteraciones de ninguna especie. A fin de alcanzar ese desiderátum en la medida posible en nuestro medio y propender al mejoramiento progresivo del producto, la leche de consumo en el municipio se clasificará en las categorías que se especifican en los artículos siguientes, y su producción, introducción, depósito, transporte y expendio se sujetarán a las prescripciones de la presente ordenanza.

ART. 2. Se considerará leche de primera calidad certificada y sólo se permitirá que en tal carácter o bajo tal denominación se introduzca al municipio, deposite, transporte, venda u ofrezca en venta dentro del mismo la leche que reúna los siguientes requisitos:

1°. Tener por lo menos 3 por ciento de materia grasa (gordura).

2°. Tener por lo menos 11.5 por ciento de sustancia seca, comprendida la materia grasa.

3°. Tener un grado de acidez no menor de 15 grados Dornic ni mayor de 20 grados.

4°. No coagularse al someterla a la ebullición, ni formar copos o grumos ni coagularse al mezclarla con dos veces su volumen de alcohol a 70 volúmenes por ciento.

5°. Sometida a cualquier procedimiento de examen, debe mostrarse perfectamente limpia.

6°. No contener en ningún momento, hasta ser entregada al consumidor, más de 60,000 microbios por c. c.

7°. Estar siempre a una temperatura de 10° o menos.

8°. Ser entregada al consumidor dentro de las 20 horas de ordeñada.

9°. No haber sufrido modificaciones de ninguna especie, debidas a la intervención de agentes físicos o químicos.

10°. Ser producida, envasada, rotulada y transportada en la forma que se indica más adelante.

La leche que no llene los requisitos 1°, 2°, o 3°, caerá en comiso, sin perjuicio de aplicarse el artículo 8, si se comprueba que ha sido adulterada. Por el exceso de acidez, se aplicará en cada caso una multa de 50 pesos.

La infracción de los requisitos 4° o 5° será penada con multa de 50 pesos cada vez. Además, a fin de que el interesado se coloque en condiciones de producir leche inobjetable a esos respectos, se prohibirá la introducción y venta de la leche en el municipio durante los cinco días subsiguientes a la comprobación. La leche caerá en comiso.

Cuando la leche presente más de 60,000 microbios por c. c., se avisará al interesado a fin de que adopte las medidas necesarias para evitar el inconveniente. El aviso se repetirá toda vez que se haga la misma comprobación. Pero la administración sanitaria podrá prohibir la introducción y venta de la leche en el municipio, si se comprueba que con frecuencia tiene más de ese número de microbios, si el número de microbios supera en grandes proporciones al indicado o si el interesado no adopta las medidas susodichas. La leche caerá en comiso.

La infracción del 7° requisito será penada con multa de 30 pesos. Si se comprueba que la leche no tiene la temperatura exigida por no haberse aplicado a los medios necesarios para conseguirlo, la multa será duplicada. La leche caerá en comiso.

La del 8° requisito será penada con multa de 50 pesos cada vez. La leche caerá en comiso.

La del 9° requisito será penada con multa de 100 pesos la primera vez, de 200 pesos la segunda y con el retiro definitivo del permiso para intervenir en cualquier forma en el comercio de leche de primera calidad certificada la tercera. La leche caerá en comiso.

La del 10° requisito, si no tiene una pena especialmente establecida, será penada con multa de 5 a 100 pesos, según la gravedad de la falta, considerándose como circunstancia agravante su repetición. Pero la administración sanitaria podrá prohibir en cualquier momento la introducción y venta de la leche, si considera que ha dejado de ofrecer suficientes garantías de salubridad.

ART. 3. Se considerará leche de primera calidad y sólo se permitirá que en tal carácter o bajo tal denominación se introduzca al municipio, deposite, transporte, venda u ofrezca en venta dentro del mismo la leche que reúna los siguientes requisitos:

1°. Tener por lo menos 2.7 por ciento de materia grasa (gordura).

2°. Tener por lo menos 10.7 por ciento de sustancia seca, comprendida la materia grasa.

3°. Tener un grado de acidez no menor de 15 grados Dornic ni mayor de 20 grados.

4°. No coagularse al someterla a la ebullición, ni formar copos o grumos ni coagularse al mezclarla con un volumen igual de alcohol a 70 volúmenes por ciento.

5°. Puesta en la cantidad de un litro, después de bien revuelta, en un recipiente cilíndrico de vidrio incoloro y de fondo plano, cuyo diámetro, sea más o menos igual a la mitad de la altura de la columna formada por la leche, no debe dejar depositar sedimento apreciable después de una hora de reposo.

6°. No contener en ningún momento, hasta ser entregada al consumidor, más de 500,000 microbios por c. c.

7°. Llegar a la ciudad a una temperatura de 15° o menos.

8°. Estar siempre a 10° de temperatura o menos, después de dos horas de su entrada a la ciudad.

9°. Ser entregada al consumidor dentro de las veinte horas de su entrada al municipio.

10°. Ser introducida, depositada, envasada, rotulada, transportada y entregada al consumidor en la forma que se indica más adelante.

La leche que no llene los requisitos 1°, 2°, o 3°, caerá en comiso, sin perjuicio de aplicarse el artículo 8°, si se comprueba que ha sido adulterada. Por el exceso de acidez, se aplicará en cada caso una multa de 30 pesos.

La infracción de los requisitos 4° o 5° será penada con multa de 30 pesos cada vez. Si la comprobación ha sido en el momento del arribo de la leche al municipio, se prohibirá su introducción y venta en el mismo durante los diez días subsiguientes, a fin de que el interesado se coloque en condiciones de enviar leche inobjetable a esos respectos. La leche caerá en comiso.

Cuando la leche contenga más de 500,000 microbios por c. c. se avisará al interesado, a fin de que adopte las medidas necesarias para evitar el inconveniente. El aviso se repetirá toda vez que se haga la misma comprobación. Pero la administración sanitaria podrá prohibir la introducción y venta de la leche en el municipio, si en tres exámenes sucesivos efectuados con 15 días de intervalo por lo menos se comprueba que el número de microbios supera en grandes proporciones al indicado o si el interesado no adopta las medidas susodichas. La leche que contenga más de 500,000 microbios caerá en comiso.

La leche que llegue a la ciudad a más de 15° de temperatura caerá en comiso.

La infracción del requisito 8° será penada con multa de quince pesos. Si se comprueba que la leche no tiene la temperatura exigida por no haberse aplicado los medios necesarios para conseguirlo, la multa será duplicada. La leche caerá en comiso.

La del requisito 9° será penada con multa de veinticinco pesos cada vez. La leche caerá en comiso.

La del décimo requisito, si no tiene una pena especialmente establecida, será penada con multa de cinco a cincuenta pesos, según la gravedad de la falta, considerándose como circunstancia agravante su repetición. Pero la administración sanitaria podrá prohibir en cualquier momento la introducción y venta de la leche, si considera que ha dejado de ofrecer suficientes garantías de salubridad.

ART. 4. La leche de primera calidad podrá ser pasteurizada. En tal caso, salvo los requisitos 6° y 9° del artículo 3, deberá reunir antes y después de la pasteurización todos los requisitos del mismo artículo y además los siguientes:

1°. No contener más de 2,000,000 de microbios por c. c. antes de ser pasteurizada.

2°. No contener en ningún momento, después de pasteurizada y hasta ser entregada al consumidor, más de 200,000 microbios por c. c.

3°. Ser entregada al consumidor dentro de las 20 horas de pasteurizada.

La primera infracción del requisito 1° de este artículo será seguida de un aviso al interesado, la segunda será penada con multa de 100 pesos, la tercera, con multa de 200 pesos y la cuarta será seguida de la prohibición de introducir o vender leche pasteurizada de primera calidad en el municipio.

La primera infracción del requisito 2° de este artículo será seguida de un aviso al interesado, a fin de que adopte las medidas necesarias para evitar el inconveniente, y las infracciones subsiguientes con una multa de 100 pesos cada vez. Pero la administración sanitaria podrá prohibir la introducción y la venta de la leche en el municipio, si en tres exámenes sucesivos efectuados con quince días de intervalo por lo menos se comprueba que el número de microbios supera en grandes proporciones al indicado o si el interesado no adopta las medidas susodichas. La leche que después de pasteurizada contenga más de 200,000 microbios por c. c. caerá en comiso.

La infracción del requisito 3° de este artículo será penada con multa de 25 pesos cada vez. La leche será comisada.

Las infracciones a los demás requisitos que debe llenar la leche pasteurizada de primera calidad tendrán las penas indicadas en el artículo 3.

ART. 5. Se considerará leche de segunda calidad y sólo se permitirá que en tal carácter o bajo tal denominación se introduzca al municipio, deposite, transporte, venda u ofrezca en venta dentro del mismo la leche que reúna los siguientes requisitos:

1°. Tener una densidad de 1,029 a 1,034, inclusive, a 15° de temperatura.

2°. Tener por lo menos 2.5 por ciento de materia grasa (gordura) en los meses de septiembre, octubre y noviembre y 2.7 por ciento en los otros meses del año.

3°. Tener por lo menos 10.5 o 10.7 por ciento, respectivamente, de sustancia seca, contada la materia grasa, según se trate del primero o segundo períodos indicados en el párrafo precedente.

4°. Tener un grado de acidez no menor de 15 grados Dornic ni mayor de 20 grados.

5°. No coagularse al someterla a la ebullición, ni formar copos o grumos ni coagularse al mezclarla con un volumen igual de alcohol a 70 volúmenes por ciento.

6°. Puesta en la cantidad de medio litro, después de bien revuelta, en un recipiente cilíndrico de vidrio incoloro y de fondo plano, cuyo diámetro sea más o menos igual a la mitad de la altura de la columna formada por la leche, no debe dejar depositar sedimento apreciable después de media hora de reposo.

7°. No contener en ningún momento, hasta ser entregada al consumidor, más de 5,000,000 de microbios por c. c.

8°. Llegar a la ciudad a una temperatura de 20° o menos.

9°. Estar siempre a 15° de temperatura o menos, después de dos horas de su entrada a la ciudad.

10°. Ser entregada al consumidor dentro de las 24 horas de su entrada al municipio.

11°. Ser introducida, depositada, envasada, rotulada, transportada y entregada al consumidor en la forma que se indica más adelante.

La leche que no llene los requisitos 1°, 2°, 3°, o 4° caerá en comiso, sin perjuicio de aplicarse el artículo 8, si se comprueba que ha sido adulterada. Por el exceso de acidez, se aplicará en cada caso una multa de 15 pesos.

La infracción de los requisitos 5° o 6° será penada con multa de 15 pesos cada vez. Si la comprobación ha sido en el momento del arribo de la leche al municipio, se prohibirá su introducción y venta en el mismo durante los veinte días subsiguientes, a fin de que el interesado se coloque en condiciones de enviar leche inobjetable a esos respectos. La leche caerá en comiso y será inutilizada.

Cuando la leche contenga más de 5,000,000 de microbios por c. c., se avisará al interesado, a fin de que adopte las medidas necesarias para evitar el inconveniente. Las tres primeras comprobaciones en tal sentido serán seguidas del mismo aviso. Pero, si después de esto, en tres exámenes sucesivos efectuados con quince días de intervalo por lo menos, se comprueba que el número de microbios supera al indicado, se prohibirá la introducción y venta de la leche en el municipio. La leche que contenga más de 5,000,000 de microbios por c. c. caerá en comiso y será inutilizada.

La leche que llegue a la ciudad a más de 20° de temperatura caerá en comiso.

La infracción del 9° requisito será penada con multa de cinco pesos. Si se comprueba que la leche no tiene la temperatura exigida por no haberse aplicado los medios necesarios para conseguirlo, la multa será duplicada. La leche caerá en comiso.

La infracción del 10° requisito será penada con multa de 15 pesos cada vez. La leche caerá en comiso y será inutilizada.

La infracción del requisito 11°, si no tiene una pena especialmente establecida, será penada con multa de cinco a treinta pesos, según la gravedad de la falta, considerándose como circunstancia agravante su repetición. Pero la administración sanitaria podrá prohibir en cualquier momento la introducción y la venta de la leche, si considera que ha dejado de ofrecer suficientes garantías de salubridad.

ART. 6. La leche de segunda calidad podrá ser pasteurizada. En tal caso, salvo los requisitos 6°, 7°, 8°, y 10° del artículo 5, deberá reunir antes y después de pasteurizada todos los requisitos de ese mismo artículo y además los siguientes:

1°. No contener más de 300,000 microbios por c. c. después de pasteurizada y antes de salir del establecimiento donde ha sufrido la pasteurización.

2°. Si ha sido pasteurizada fuera del municipio, no contener más de 400,000 microbios por c. c. en el momento de llegar a él.

3°. Ser entregada al consumidor dentro de las 24 horas de la pasteurización.

La primera infracción de los requisitos 1° y 2° de este artículo será seguida de un aviso al interesado. En las infracciones subsiguientes se incurrirá en multa de 100 a 500 pesos, según la cantidad de leche de que se trate y la gravedad del caso, considerándose como circunstancia agravante la repetición de la falta. Si la leche ha sido pasteurizada fuera del municipio, en lugar de las multas indicadas, podrá prohibirse su introducción y venta en él durante 1 a 30 días, teniendo en cuenta las mismas circunstancias.

La infracción del requisito 3° de este artículo será penada con quince pesos de multa cada vez. La leche caerá en comiso y será inutilizada.

La de los otros requisitos dará lugar a las medidas y penas indicadas en el artículo 5.

ART. 7. Se prohibe la introducción al municipio y el depósito, transporte, venta u ofrecimiento en venta dentro del mismo, de leche, cualquiera sea su categoría, que tenga color, olor, gusto o consistencia anormales, o que contenga sangre o pus.

Las infracciones del presente artículo serán penadas con multa de 15 a 100 pesos o uno a seis días de arresto, según la gravedad del caso, considerándose la repetición de la falta como circunstancia agravante.

A quien incurra dos veces en las penas más graves se le retirará por el término de un año el permiso para intervenir en cualquier forma en el comercio de lechería. La leche será comisada e inutilizada en todos los casos.

ART. 8. Igual prohibición que la expresada en el artículo 7 rige para la leche de cualquier categoría a la que se haya sustraído en cualquier forma una parte de su crema o gordura o se haya agregado agua u otra sustancia cualquiera, comprendidas las llamadas "conservadoras."

Los infractores del presente artículo incurrirán en la pena de cien pesos de multa o seis días de arresto la primera vez, doscientos de multa o doce días de arresto la segunda y retiro definitivo del permiso para intervenir en cualquier forma en el comercio de lechería la tercera. La leche caerá en comiso.

ART. 9. Salvo las leches de que se trata en los artículos 13 y 14, se prohibe la introducción al municipio y el depósito, transporte, venta u ofrecimiento en venta dentro del mismo de toda leche que por sus condiciones no esté comprendida en alguna de las categorías especificadas en los artículos 2, 3, 4, 5 y 6, respectivamente, de esta ordenanza, bajo pena de 100 pesos de multa a la primera infracción, 200 a la segunda, retiro definitivo del permiso para intervenir en cualquier forma en el comercio de lechería a la tercera y comiso de la leche en todos los casos.

ART. 10. Se prohibe introducir leche al municipio y depositarla, transportarla, venderla u ofrecerla en venta dentro del mismo en otro carácter o bajo otras denominaciones que los indicados en los artículos 2, 3, 4, 5 y 6 y en los correlacionados con ellos, ni en forma que pueda inducir a error acerca de la categoría a que pertenece la leche según las prescripciones de la presente ordenanza. Se exceptúan, en lo que se refiere al carácter y denominación con que se presenten, las leches de que se trata en los artículos 12, 13 y 14, pero estas leches y todas las análogas que puedan destinarse al consumo, cualesquiera sean su modo de preparación, modificaciones, clases o usos, deberán ser introducidas al municipio y depositarse, transportarse, venderse u ofrecerse en venta dentro del mismo, indicando en la forma establecida más adelante a qué categoría de las especificadas en los artículos susodichos pertenecen o a cual de esas categorías pertenece la leche con que han sido preparadas.

A los que infrinjan el presente artículo se les decomisará la leche y aplicarán las penas establecidas en el artículo 9.

ART. 11. Las leches pasteurizadas, además de las condiciones establecidas en los artículos 4 y 6, deberán satisfacer las siguientes:

1°. Haber sido libradas de sus impurezas por algún procedimiento mecánico que no separe completamente la crema.

2°. Haber sido sometidas en seguida, en toda su masa, por lo menos a 85° de temperatura durante un minuto.

3°. Haber sido enfriadas, inmediatamente después de calentadas, a 10 o 15 grados de temperatura o menos, según se trate respectivamente de leche de primera o segunda calidad.

4°. Haber sufrido las operaciones antedichas dentro de las catorce horas de ordeñadas.

5°. No haber sido calentadas o pasteurizadas por segunda vez.

6°. Haber sido sometidas a esas operaciones en aparatos aprobados por la administración sanitaria.

No se permitirá la introducción ni venta de leche pasteurizada que no satisfaga estos requisitos, y quien infrinja las disposiciones de este artículo, después de un primer aviso, incurrirá en el decomiso de la leche y en multa de 100 a 200 pesos, según la gravedad del caso, considerándose circunstancia agravante la repetición de la falta.

ART. 12. Sólo se tendrá por leche esterilizada la que después de limpiada en la forma prescrita en el artículo 11 haya sido sometida dentro de las catorce horas de ordeñada a algún procedimiento de esterilización por el calor de reconocida eficacia y cuyo envase se haya cerrado herméticamente durante el calentamiento y se mantenga igualmente cerrado hasta su entrega al consumidor.

Se prohibe la introducción y la venta de leche esterilizada que no llene las condiciones aquí establecidas, bajo pena de comiso del producto y multa de 100 a 200 pesos cada vez, según la gravedad del caso, considerándose como circunstancia agravante la repetición de la falta.

ART. 13. Las leches maternizadas o humanizadas y las análogas, especialmente destinadas a la alimentación de los niños o de enfermos o convalecientes, deberán ser preparadas con leche que satisfaga por lo menos los cinco primeros requisitos especificados en el artículo 5, que no se halle comprendida en los artículos 7 y 8 y librada de sus impurezas en la forma prescrita en el artículo 12. Todas estas leches deberán ser esterilizadas en la forma establecida en el artículo 12.

Los que infrinjan el presente el artículo incurrirán en las penas indicadas en el artículo 12 o en los artículos 7 u 8, según los casos.

ART. 14. Las leches especiales fermentadas (Kefir, etc.) deberán ser preparadas con leche que satisfaga por lo menos los cinco primeros requisitos especificados en el artículo 5, no se halle comprendida en los artículos 7 y 8 y esterilizada en la forma prescrita en el artículo 12, correspondiendo a las infracciones de lo aquí establecido las penas indicadas en el artículo 13.

ART. 15. Se prohibe introducir al municipio y depositar, transportar, vender u ofrecer en venta dentro del mismo, leche que sea la mezcla de distintos ordeños o de partidas de leche recibidas en horas distantes entre sí. La leche ordeñada o recibida por la mañana no debe ser mezclada con la ordeñada o recibida por la tarde, ni inversamente.

Los que infrinjan el presente artículo incurrirán en el comiso de la leche y en multa de 150, 100 o 50 pesos, respectivamente, cada vez, según se trate de leche de primera calidad certificada, de primera calidad o de segunda calidad.

ART. 16. Quien deliberadamente o sin cerciorarse primero de la calidad a que pertenece la leche según las prescripciones de la presente ordenanza, la introduzca, deposite, transporte, venda u ofrezca en venta en el municipio como de mejor calidad

que a la que realmente pertenece, incurrirá en multa de 100 pesos la primera vez, doscientos pesos la segunda y en el retiro definitivo del permiso para intervenir en cualquier forma en el comercio de lechería la tercera vez.

ART. 17. Se prohibe congelar la leche o agregarle leche congelada, bajo pena de 100, 50 o 25 pesos de multa, respectivamente, según se trate de leche de primera calidad certificada, de primera calidad o de segunda calidad.

Fig. 3



Fig. 1

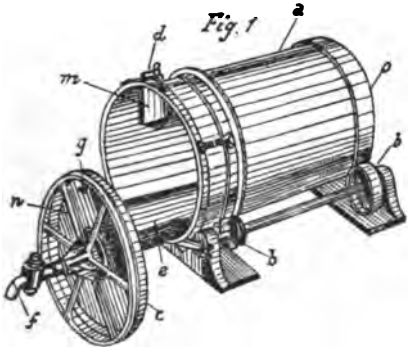


Fig. 4

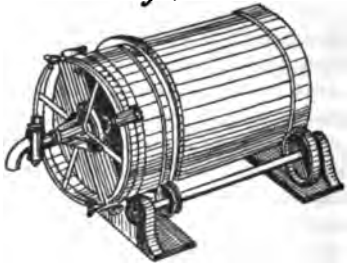


Fig. 2

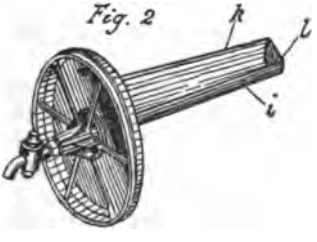
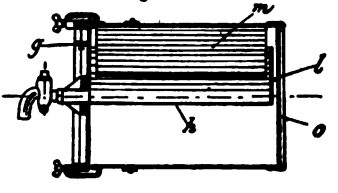


Fig. 5



ART. 18. Salvo los artículos 7, 8, 16 y 17, los demás del presente capítulo no se aplican a la leche producida en los tambos urbanos y entregada al consumidor inmediatamente de ordeñada.

CAPÍTULO II. CONDICIONES DE LOS ENVASES, RECIPIENTES, ÚTILES, APARATOS, MÁQUINAS EN GENERAL.

ART. 19. Para el envase, medida y manipulaciones de la leche sólo se permitirá el uso de recipientes y útiles de hierro o acero con estañado grueso y de botellas devidrio incoloro. Se prohibe expresamente usar recipientes de cobre, zinc, latón, plomo hierro emplomado o madera.

Esos recipientes deberán ser de limpieza y desinfección fáciles. Los metálicos serán sin costura y tendrán sus ángulos redondeados y las botellas serán de fondo plano. Los de dos litros o más de capacidad tendrán la boca suficientemente amplia como para permitir introducir cómodamente la mano de un hombre adulto. Los más pequeños serán de tal forma y disposición que su interior pueda limpiarse a cepillo fácil y completamente.

Los recipientes usados para medir la leche deben estar provistos de asa o mango apropiados, de tal modo que la mano del que los maneja no se ponga en contacto con la leche.

ART. 20. Las tapas de los envases y recipientes deben llenar las mismas condiciones que éstos, especificados en el precedente artículo.

Si se trata de envases empleados en el transporte de la leche, serán de cierre hermético y la tapa recubrirá los bordes de su boca o abertura. Si de envases especialmente destinados a tenerla en depósito en locales fijos, las tapas deberán recubrir por arriba y por fuera la boca y el cuello del recipiente y podrán no ser ajustadas.

Se prohibe expresamente usar trapos, papel, paja, madera o materias análogas y aros de goma que contenga plomo o estén agrietados, para tapar los recipientes o como intermediarios para cerrarlos.

Para el cierre de botellas se permite el uso de tapas de loza, porcelana y vidrio y de placas de papel especialmente preparadas y que deberán usarse una sola vez.

ART. 21. Los recipientes de que se trata en el artículo 19 y las tapas deben hallarse siempre en buen estado de conservación, es decir, en condiciones que permitan sus fácil limpieza y desinfección.

Se prohibe expresamente el uso de los que tengan su superficie interna oxidada, así como de los que por sus abolladuras u otros desperfectos no se hallen en las condiciones susodichas.

ART. 22. Las cantillas o robinetes de los recipientes y, en general, todas las que se hallen en contacto con la leche, serán metálicas y bien cubiertas interior y exteriormente por una capa gruesa de estaño, de modo que en ningún caso pueda formarse cardenillo. Interior y exteriormente serán perfectamente lisas y dispuestas de tal manera que su limpieza y desinfección sean fáciles.

ART. 23. Los aparatos, máquinas, grandes depósitos, etc., empleados en la manipulación o tratamiento de la leche deben ser en todas las partes que entren en contracto con ella de material impermeable y perfectamente liso. Se prohibe expresamente emplear en esas partes, cobre, zinc, latón, plomo, hierro emplomado o madera.

ART. 24. No se expedirán permisos para dedicarse en cualquier forma al comercio de lechería, sin cerciorarse primero de si el interesado tiene todos los elementos indicados en este capítulo, y que deba emplear, en las condiciones aquí establecidas.

Los infractores de los artículos 19, 20, 21 o 22 incurrirán en multa de 5 a 20 pesos, según la gravedad de la falta, considerándose como circunstancia agravante su repetición. Además, los recipientes, útiles, tapas, etc., mencionados en esos artículos, serán marcados la primera vez que se hallen fuera de las condiciones exigidas y destruidos la segunda vez.

A los infractores del artículos 23 se les retirará el permiso correspondiente hasta tanto se pongan en las condiciones exigidas.

CAPÍTULO III. ASEO DE RECIPIENTES, ÚTILES Y CUIDADO DE LA LECHE EN GENERAL.

ART. 25. Los recipientes, tapas, máquinas, útiles, etc., a que se refiere el Capítulo II, deberán hallarse siempre limpios por dentro y fuera y no usarse para transportar, guardar o medir otra sustancia que la leche, ni, en general, para otros fines que aquellos a que están destinados.

Se prohibe especialmente beber en las medidas o recipientes, bajo pena de diez pesos de multa.

Se deja establecido expresamente que se considerará sucio todo recipiente, útil, etc., de los referidos en este artículo, que tenga olor a leche agria o cualquier olor extraño, aunque en él no se noten restos de leche o de otras sustancias.

ART. 26. La limpieza de los recipientes, utensilios, etc., a que se refiere el artículo 25, debe efectuarse tratándolos primero con una solución caliente y extendida de soda o con lechada de cal, enjuagándolos abundantemente después con agua caliente, de manera que no quede resto alguno de soda o cal, y arrojando finalmente un chorro de agua hirviendo sobre toda su superficie interna. En seguida de limpiados, se pondrán boca abajo en un sostén destinado a ese efecto (escurridor) y en un lugar libre de moscas, de polvo y de toda otra causa de suciedad o contaminación. No deben colocarse boca abajo sobre el suelo. Teniendo vapor de agua a disposición, en lugar de efectuar la esterilización con agua hirviendo, puede hacerse con un chorro de vapor. Lo mismo, si se dispone de cualquier otro medio de esterilización, éste puede ser aplicado en lugar del agua hirviendo.

ART. 27. Toda persona que se dedique al comercio de lechería, que reciba de otra un recipiente con leche, está obligada a devolvérselo limpio, bajo pena de cinco pesos de multa. Exímese de esta obligación a los que reparten leche a domicilio recibida de comerciantes o empresas con establecimientos donde pueda hacerse la limpieza instalados en la capital y siempre que la reciban en los mismos envases que han de servir para el reparte, no la sometan después a trasvasamientos de ninguna especie y devuelvan a los mismos los tarros vacíos en seguida de terminado el reparto. De acuerdo con lo que antecede, en las estaciones ferroviarias no deberá presentarse a embarque ningún envase que no esté limpio, ni deben transportarse dentro del municipio otros envases vacíos y sin limpiar más que los que se vayan vaciando o se hayan vaciado en el reparto a domicilio.

No se permitirá la salida de la Capital de ningún recipiente sucio.

ART. 28. Los recipientes que contengan leche deberán estar siempre perfectamente cerrados con su tapa correspondiente, salvo durante los momentos en que se eche o extraiga leche, bajo pena de cinco pesos de multa.

ART. 29. No se permite trasvasar la leche de un recipiente a otro, ni someterla a manipulaciones de ninguna especie, en la vía pública, en las estaciones ferroviarias, en corralones, ni, en general, al aire libre. Estas operaciones deben efectuarse en un local especialmente destinado a ese efecto. Se exceptúan los casos en que, por rotura del recipiente, sea necesario echar su contenido a otro, a fin de evitar la pérdida de la leche.

Los infractores de este artículo incurrirán en multa de diez pesos.

ART. 30. Se prohibe soplar con la boca la superficie de la leche para apartar la crema o cualquier cosa, o hacer tal operación con los dedos.

ART. 31. Los recipientes que contengan leche, aunque estén cerrados, no deben dejarse expuestos en las veredas u otros lugares de la vía pública, ni al polvo o a las moscas, ni al sol, ni a cualquier causa de suciedad o contaminación.

ART. 32. De los tanques o depósitos provistos de canilla la leche deberá extraerse por esta última, y nunca por la boca o abertura superior.

ART. 33. Al lado de todo tanque con canilla debe haber un soporte especial para colocar el recipiente del comprador mientras se echa en él la leche que se va midiendo.

ART. 34. Con la leche no deberá guardarse más que manteca, crema y otros preparados o derivados de la leche incapaces de comunicarle sus olores.

ART. 35. Los infractores de los artículos 28, 29, 30, 31 o 32 incurrirán en multa de 100 pesos.

ART. 36. Para mantener fresca la leche podrán emplearse cámaras frigoríficas, aparatos refrigeradores, heladeras o cubas con hielo, que deberán ser de limpieza y desinfección fáciles y hallarse siempre en buenas condiciones de conservación y de aseo.

Las heladeras y cubas deberán tener revestimiento metálico interior inoxidable y estar barnizadas o pintadas con pintura impermeable y blanca o de color claro.

No se otorgarán los permisos correspondientes, a quienes no tengan estos elementos de refrigeración en la medida necesaria para la cantidad de leche con que operen o comercien y en las condiciones aquí establecidas. A los que infrinjan el presente artículo se les aplicará 10 pesos de multa y no se les permitirá la venta de leche hasta que se coloquen en las condiciones exigidas.

ART. 37. En todo local donde se limpien recipientes deberá haber un servicio de agua caliente, capaz, por lo menos, de producir en una sola sesión o en un chorro continuo una cantidad de agua hirviente igual a la mitad de la cantidad de leche con que se opere o comercie. Esta proporción no regirá para las fábricas o usinas, que deberán tener instalaciones especiales para la limpieza de los recipientes, aprobados por la administración sanitaria.

La falta de cumplimiento de este artículo dará lugar a las medidas y penas indicadas en el artículo 36.

ART. 38. Toda el agua usada en los establecimientos de lechería deberá ser potable.

Esta disposición comprende aún a los establecimientos productores o remitentes de leche de fuera del municipio, a quienes no se les permitirá introducir sus productos, so pena de comisárselos a su llegada, mientras la administración sanitaria no se cerciore en lo posible de la calidad de las aguas que emplean.

ART. 39. Los recipientes en que se introduce la leche al municipio deben venir cerrados bajo sello, que para los envases metálicos será de plomo, de modo que no puedan ser abiertos sin que ello se note, desde el momento en que el remitente los entrega a quien haya de transportarlos hasta aquel en que los recibe el consignatario.

La leche que llegue en recipientes no sellados o cuyo sello haya sido violado caerá en comiso.

ART. 40. En las usinas o fábricas de lechería, las leches de distintas calidades deberán ser tratadas aparte, en locales o secciónes especiales y separadas para cada una, provistos de su maquinaria y equipo correspondientes completos. Lo mismo para la fabricación de manteca, deberá haber en ellas un local o sección especial y aparte, donde se harán todas las operaciones, comprendido el descremado de la leche y el depósito de la leche destinada a descremarse.

Los infractores del presente artículo incurrirán en multa de 100 a 500 pesos, según la gravedad de la falta. Si los establecimientos en que él se infrinja se hallan fuera de la Capital, no se les permitirá la introducción de leche al municipio, so pena de decomisársela, por uno a veinte días, según la gravedad de la falta, a no ser que prefieran abonar la multa que les correspondería si se hallaran dentro de ella.

Al establecimiento que no tenga el local o sección especial y aparte para tratar una determinada calidad de leche, no se le permitirá vender o introducir leche de esa calidad. Al que fabrique manteca y no tenga un local o sección especial y aparte para ello, no se le permitirá la introducción o venta de ninguna clase de leche.

CAPÍTULO IV. CONDICIONES ESPECIALES DE ENVASE Y ROTULADO DE LA LECHE SEGÚN SU CALIDAD.

ART. 41. La leche de primera calidad certificada será entregada al consumidor en botellas llenadas, cerradas y selladas en el lugar de producción y provistas de cápsula que proteja la tapa y la boca de la botella.

Previa solicitud del interesado, la administración sanitaria podrá permitir el uso de recipientes metálicos, cuando se trate de remitir a un mismo consumidor una cantidad de leche mayor de veinte litros cada vez.

Botellas y recipientes metálicos serán entregados con el cierre intacto al consumidor, es decir, con su sello entero.

Los infractores de este artículo incurrirán en multa de cincuenta pesos. La leche de las botellas o recipientes metálicos que se hallen con el sello roto antes de entregarlas al consumidor caerá en comiso.

ART. 42. Los recipientes de que se trata en el artículo anterior deberán llevar impresa en las cápsulas o en etiquetas pegadas a los mismos, en letras negras y fácilmente legibles, la siguiente leyenda, en que constará el día y la hora en que ha sido ordeñada la leche:

Leche de primera calidad certificada.
Vigilada desde su producción por la Administración Sanitaria.
Especial para niños y enfermos.
Puede consumirse cruda.
Ordeñada el día .... a las ....

Las cápsulas y las etiquetas deberán ser blancas.

ART. 43. Los recipientes en que se introduzca la leche de primera calidad al municipio deberán venir provistos de una etiqueta atada o pegada, respectivamente, según sean envases metálicos o de vidrio, de ocho por cuatro centímetros de dimensión por lo menos y de color blanco, en que consten en letras de molde, de color rojo y bien legibles, la calidad de la leche, el número de litros que contiene el recipiente, el día y hora de embarque con destino a la capital, el nombre y apellido de su productor, el de la estación ferroviaria de donde la leche es expedida, el nombre del destinatario y la dirección de su establecimiento en Buenos Aires, en la siguiente forma:

Leche de primera calidad.
Litros ....
Embarcada en ...., el día .... a las .....
Productor .....
Destinatario ..... Calle ....., No...

Cuando el remitente sea alguna empresa o establecimiento que recoja la leche de distintos productores para enviarla a Buenos Aires, será su nombre el que deberá figurar en la etiqueta, en lugar del del tambero o productor, precedido de la palabra "Remitente."

Cuando la leche sea pasteurizada o esterilizada, deberá constar ésto en la etiqueta, poniendo en su primer renglón, respectivamente: "Leche de primera calidad pasteurizada" o "Leche de primera calidad esterilizada."

ART. 44. Cuando la leche de primera calidad se introduzca al municipio para ser pasteurizada, la etiqueta de que se trata en el artículo 43 será amarilla y la leyenda de la misma estará impresa en letras negras. En ésta deberá constar el destino inmediato de la leche, poniendo en su primer renglón: "Leche de primera calidad para pasteurizar."

ART. 45. En el reparto a domicilio, la leche de primera calidad deberá ser transportada y entregada al consumidor en recipientes metálicos o de vidrio cerrados y sellados en el lugar donde hayan sido llenados.

Los envases serán entregados al consumidor con su sello intacto, bajo pena de veinticinco pesos de multa.

ART. 46. Los recipientes de que se trata en el artículo precedente deberán estar provistos de etiqueta blanca, pegada al envase en lugar visible, con la siguiente leyenda, en letras de molde, rojas y fácilmente legibles, donde conste el nombre del vendedor y la dirección de su establecimiento, o, si no tiene establecimiento, su domicilio:

Leche de primera calidad.
Los niños y enfermos deben consumirla hervida.
(Aquí el nombre y apellido del vendedor.)
(Aquí la dirección de su establecimiento, o, a defecto de éste, de su domicilio.)

Cuando la leche sea pasteurizada, deberá constar ésto en la etiqueta y además el nombre de la fábrica o usina donde haya sido pasteurizada y el día y la hora en que e efectuó la operación, resultando así la leyenda de la etiqueta en la siguiente forma:

Leche de primera calidad pasteurizada.
Los niños y enfermos deben consumirla hervida.
Pasteurizada por o en .... el día .... a las ....
(Aquí el nombre y apellido del vendedor.)
(Aquí la dirección de su establecimiento, o, a defecto de éste, de su domicilio.)

Los dos primeros renglones de la leyenda (donde se indica la calidad de la leche y la manera cómo debe ser, consumida), tanto para la leche cruda como pasteurizada, serán en letras de doble tamaño que el resto de la misma.

ART. 47. Previa solicitud en cada caso del interesado, la Administración Sanitaria podrá permitir el uso de tanques con canilla para el transporte de la leche de primera calidad en el reparto a domicilio, siempre que el interesado y esos tanques satisfagan todas las condiciones establecidas en el artículo 82 y que además los tanques sean sellados en el lugar donde se llenen y esten dispuestos de tal modo que la leche pase del tanque al recipiente del consumidor sin ponerse en contacto con al aire.

En tal caso, los tanques llevarán en la forma indicada en el artículo 51 un letrero indicador de la calidad de la leche y de la manera cómo debe ser consumida.

Si se trata de leche pasteurizada en la Capital, los tanques deberán ser llenados en el lugar de pasteurización.

ART. 48. Los recipientes en que se introduzca la leche de segunda calidad al municipio deberán venir provistos de una etiqueta atada al envase, de ocho por cuatro centímetros de dimensión por lo menos, de color verde, y en que consten, en letras de color negro y bien legibles, los datos especificados en el artículo 43 y en la forma de leyenda allí indicada.

Si se trata de leche esterilizada, la etiqueta vendrá pegada a las botellas, en lugar visible, y será blanca, con la escritura en verde.

ART. 49. Cuando la leche de primera calidad se introduzca al municipio para ser pasteurizada, la etiqueta de que se trata en el primer párrafo del artículo precedente será amarilla y la leyenda de la misma estará impresa en letras negras. En ésta deberá constar el destino inmediato de la leche, poniendo en su primer renglón; "Leche de segunda calidad para pasteurizar."

ART. 50. Para el reparto a domicilio de la leche de segunda calidad, la leche será transportada en tanques con canilla o robinete, de la capacidad que se quiera, o en recipientes o tarros de ocho litros de capacidad como máximum.

Los que deseen entregar envasada esta leche al consumidor, deberán usar botellas o envases metálicos cerrados y sellados en el lugar donde hayan sido llenados. En tal caso, los recipientes serán entregados al consumidor con su sello intacto, bajo pena de cinco pesos de multa.

ART. 51. Los recipientes de que se trata en el primer párrafo del artículo precedente deberán llevar pintado, estampado, grabado o soldado sobre el costado, en letras de molde de tres centímetros de altura y medio centímetro de grueso por lo menos, el siguiente letrero:

Segunda calidad.
Consúmase hervida.

Si se trata de leche pasteurizada, el letrero será así:

Segunda calidad pasteurizada.
Consúmase hervida.

Estos letreros serán de color que resalte sobre el del recipiente, y por su forma y lugar deberán ser bien visibles y legibles. En los tanques o recipientes con canilla deberán hallarse de 5 a 10 centímetros sobre la canilla.

ART. 52. Los recipientes de que se trata en el segundo párrafo del artículo 50 deberán estar provistos de etiqueta blanca, pegada en lugar visible, con la siguiente leyenda, en letras de molde, verdes y fácilmente legibles, donde conste el nombre del vendedor y la dirección de su establecimiento, o, si no tiene establecimiento, su domicilio:

Leche de segunda calidad.
Consúmase hervida.
(Aquí el nombre y apellido del vendedor).

(Aquí la dirección de su establecimiento o, a defecto de éste, de su domicilio.)

Si se trata de leche pasteurizada, la leyenda será modificada de acuerdo con lo dicho en el artículo 46.

Los dos primeros renglones de la leyenda (donde se indica la calidad de la leche y la manera cómo debe ser consumida), tanto para la leche creuda como pasteurizada, serán en letras de doble tamaño que el resto de la misma.

ART. 53. La leche pasteurizada no debe ser guardada, depositada, ofrecida en venta, ni vendida o entregada al consumidor en recipientes cerrados y sellados, a menos que haya sido envasada en esa forma en el lugar donde ha sido pasteurizada.

ART. 54. La administración sanitaria, cuando lo estime necesario para el mejor cumplimiento de esta ordenanza, y previniendo a los interesados con cuatro meses de anticipación, podrá exigir que los recipientes metálicos lleven, además de los distintivos aquí establecidos, una raya de color que esté de acuerdo con esos distintivos. También podrá exigir, previniendo a los interesados con cuatro meses de anticipación, que los envases de otras leches o derivados, no mencionadas en este capítulo, lleven etiquetas o letreros en la forma que más convenga al mejor cumplimiento de la presente ordenanza.

ART. 55. Las etiquetas atadas de que deben venir provistos los envases en que se introduce la leche a la capital deberán ser guardadas por lo menos durante dos meses por los comerciantes que abran los recipientes y tenerse siempre arregladas en orden cronológico. Arregladas en esta forma serán puestas a disposición de los inspectores de la Administración Sanitaria, toda vez que éstos lo soliciten.

ART. 56. Todo el que venda leche dentro del municipio deberá llevar un libro foliado, sellado por la administración sanitaria y convenientemente dispuesto, en que anotará diariamente, en orden cronológico y sin dejar renglones en blanco, en seguida de recibir cada partida de leche, los siguientes datos relativos a la misma: fecha y hora en que recibe la leche, número de litros recibidos y número de tarros y botellas en que la recibe, calidad de la leche (si es de primera calidad certificada, de primera calidad o de segunda según las disposiciones de la presente ordenanza, y si es cruda, pasteurizada, etc.), nombre del tambero, productor o empresa de quien la recibe, estación ferroviaria donde la leche es embarcada para remitirla a Buenos Aires y ubicación del tambo o establecimiento de donde se le remite o adonde va a buscarla, si la compra en esta Capital.

Este libro se hallará siempre en el establecimiento del vendedor, o, si éste no tiene establecimiento, deberá llevarlo en el carro.

ART. 57. Todo el que dentro del municipio venda leche al por mayor o para revender, deberá llevar un libro foliado, sellado por la administración sanitaria y convenientemente dispuesto, en que anotará, en orden cronológico y sin dejar renglones en blanco, en seguida de entregar cada partida de leche, los siguientes datos relativos a la misma: fecha y hora de la entrega, número de litros de leche y de tarros y botellas en que la entrega, calidad de la leche (en la forma indicada en el artículo precedente), nombre del comprador y dirección de su establecimiento, o de su domicilio, si no tiene establecimiento.

Este libro deberá hallarse siempre en el establecimiento del que vende leche al por mayor o para revender.

Las anotaciones especificadas en este artículo podrán llevarse con las de que se trata en el artículo precedente en un mismo libro convenientemente dispuesto.

ART. 58. Todo tambero o productor que remita a la Capital leche de primera calidad certificada o leche de primera calidad y toda firma o empresa que remita leche de cualquier clase procedente de más de un productor, o pasteurizada o sometida a otras operaciones después de recibida del productor, deberá llevar un libro en la forma indicada en los artículos 56 y 57, en que anotará, en la forma allí también indicada, cada partida de leche enviada a la Capital y los siguientes datos relativos a la misma: fecha y hora en que remite la leche a la estación de embarque, número de litros remitidos y número de tarros y botellas en que la remite, calidad de la leche, nombre de la persona, firma o empresa a quien la remite y dirección de su establecimiento. Cuando remita leche a varios consignatarios, la leche enviada a cada uno se considerará como una partida distinta a los efectos de las anotaciones.

ART. 59. La leche que llegue a la Capital fuera de las condiciones establecidas en los artículos 43, 44, 48, o 49 caerá en comiso.

Los infractores de los artículos 42 o 45 incurrirán en multa de 25 pesos y comiso de la leche; los del artículo 46, en 15 pesos de multa y comiso de la leche; los del artículo 50, en 10 pesos de multa y comiso de la leche; y los de los artículos 56 o 57, en 50 pesos de multa.

Los infractores de los artículos 51 o 52 incurrirán en cincuenta pesos de multa la primera vez, cien pesos la segunda y en el retiro definitivo del permiso para intervenir en cualquier forma en el comercio de lechería la tercera. La leche será comisada en todos los casos.

A los infractores del artículo 53 se les comisará la leche y se les aplicará una multa de cincuenta pesos, si se trata de leche de primera calidad, y de 25 pesos, si de segunda calidad.

A los del artículo 55 se les comisará la leche y se les aplicará una multa de veinticinco pesos la primera vez, 50 la segunda y 100 pesos la tercera y las sucesivas.

A los del artículo 58 no se les permitirá la introducción de leche al municipio durante 5 a 15 días, según la gravedad de la falta, para juzgar la cual se tendrá en cuenta también la calidad de la leche. El interesado podrá cambiar esa pena por el pago de una multa de 50 a 150 pesos, según la gravedad de la falta.

ART. 60. La administración sanitaria no otorgará los permisos correspondientes, sin comprobar primero si el interesado dispone de los elementos necesarios para dar cumplimiento a lo establecido en el presente capítulo, en las partes que le atañen.

CAPÍTULO V. LOCAL DE MANIPULACIONES, DEPÓSITO Y PREPARACIÓN DE LA LECHE PARA LA VENTA.

ART. 61. Toda persona, firma o empresa que se dedique al comercio de lechería dentro del municipio, o sea, que compre o que venda leche para comerciar, está obligada a tener un local especial para depositar en él la leche y para efectuar en él las manipulaciones y preparación de la leche para la venta, entendiéndose por depositar aún el simple hecho de guardarla por cualquier tiempo y por manipulación o preparación, aún el simple trasvasamiento de la leche de un recipiente a otro o la simple operación de limpiar un tarro, recipiente o útil de cualquier clase, empleado en el comercio de lechería.

Cuando esta ordenanza se refiere al establecimiento de un comerciante de lechería dentro de la Capital, debe entenderse que habla del local de que se trata en el presente artículo, si el comerciante no tiene otro establecimiento. Asimismo, en el curso de esta ordenanza, y tratándose de lo que esté dentro del municipio, se llamará simplemente local de manipulaciones al local de que se trata en el presente artículo.

ART. 62. El local de manipulaciones no podrá estar en casas de inquilinato, ni en casas antihigiénicas.

A quince metros de él no deberá haber caballerizas, gallineros, ni ninguna instalación semejante o capaz de producir malos olores, de atraer las moscas en gran número o de cargar la atmósfera de polvos que puedan llegar hasta el local.

El espacio libre que lo rodea estará cubierto de piso sólido, de material impermeable y superficie lisa, por lo menos en un ancho de tres metros.

ART. 63. El local de manipulaciones constará de dos piezas de material (obra de fábrica), secas, con abundante luz natural, bien ventiladas, frescas, sin malos olores, suficientemente amplias como para que las operaciones a que están destinadas puedan hacerse cómodamente en buenas condiciones y sin amontonamiento de cosas, dispuestas de tal modo que su limpieza y desinfección sean fáciles y que la leche se exponga lo menos posible a contaminaciones y mantenidas siempre en buen estado de conservación y aseo. En cuanto a la construcción, disposición, utilaje y mantenimiento de las dos piezas que constituyen el local de manipulaciones, deberán llenarse por lo menos las siguientes condiciones:

1°. Tendrán piso sólido, impermeable y liso, de cemento, baldosa, mosaico o material análogo, con las junturas bien tomadas con cemento, y provisto de desagüe dispuesto de manera que no se desprendan emanaciones en el interior del recinto.

2°. Las paredes estarán revestidas hasta dos metros de altura por lo menos, de baldosas esmaltadas o piedras análogas, de color blanco, con las junturas bien tomadas con cemento impermeable.

3°. El resto de las paredes será de superficie lisa y pintado con pintura blanca e impermeable.

4°. El cielo raso será sólido (no de papel), liso y pintado de blanco.

5°. Los ángulos formados por las paredes entre sí y con el piso serán redondeados.

6°. Cada pieza tendrá por lo menos una ventana o una puerta, suficientemente amplias, abiertas sobre la calle o un patio abierto o sobre un zaguán que dé a la calle o a un patio abierto, a no ser que tengan claraboyas que aseguren la entrada de la luz y la ventilación necesarias.

7°. Sus aberturas exteriores estarán provistas de tela metálica, que impida la entrada de las moscas.

8°. Se comunicarán directa e inmediatamente entre sí, por una puerta que se cierre automáticamente y que se abrirá sólo para pasar.

9°. Las piezas no estarán en comunicación directa con letrinas.

10°. Si se comunican directamente con alguna habitación, sea ésta dormitorio o no, las puertas de comunicación estarán provistas de algún mecanismo de cierre automático y sólo se abrirán para el paso de las personas.

11°. No serán usadas como dormitorios, ni para habitación de enfermos, ni para ningún fin doméstico.

12°. Habrá en cada pieza una escupidera con agua.

13°. Las tapas de las mesas que sea necesario tener en ellas serán de material sólido, liso, impermeable e inoxidable. El resto de las instalaciones, aparatos y muebles (mesas, bancos, estantes, dispositivos para tener los recipientes, escurridores, etc.) serán del mismo material, o, en su defecto, estarán pintados con pintura impermeable y blanca.

14°. El pintado del local y de sus instalaciones, muebles, etc., se renovará en cuanto se halle manchado o en mal estado de conservación.

15°. Los recipientes vacíos y limpios que se hallen en el local de manipulaciones deberán estar siempre tapados, o, si están destapados, colocados boca abajo en escurridores u otros dispositivos apropiados.

16°. El local será abundantemente ventilado todos los días, y él y todo lo que haya dentro de él estarán siempre libres de polvo, telarañas, tierra y restos o resíduos de resíduos de cualquier especie.

17°. No debe echarse o extenderse sobre el piso ninguna sustancia pulverulenta, tal como aserrín, arena, etc.

18°. Para la limpieza no se usará nunca la escoba seca ni el plumero. Debe usarse el trapo y el lavado.

19°. En ninguna de las piezas del local deben permanecer niños ni otras personas que no tengan que hacer en el manejo de la leche.

20°. No deben entrar a ellas animales domésticos de ninguna especie.

ART. 64. Una de las piezas del local será especial y exclusivamente destinada al depósito, envase y preparación de la leche para la venta.

En ella no se procederá a la limpieza de recipientes ni utensilios.

Deberá estar provista de los elementos necesarios para mantener fría la leche que se guarde.

En ella no podrán guardarse más que la leche, derivados de la misma incapaces de comunicarle olores extraños, huevos frescos y otros productos de granja en envases herméticamente cerrados. Ni deberá haber en ella más que lo que sea necesario para los fines a que está destinada, ni ningún útil, tarro o recipiente vacío que no esté limpio y seco.

ART. 65. La otra pieza del local de manipulaciones será especial y exclusivamente destinada a la limpieza de recipientes y utensilios.

En ella no se guardará la leche, ni ninguno de los productos que deben y pueden estar en la otra, según lo dicho en el artículo precedente.

Estará provista de una pileta para el lavado, de material impermeable y liso, de dimensiones proporcionadas a las necesidades, convenientemente dispuesta para aquel fin y con servicios de agua corriente, caliente y fría.

En esta pieza no deberá haber más que los elementos necesarios para la limpieza y secado de los recipientes y utensilios, recipientes y utensilios listos para limpiarse y los ya limpios, durante el tiempo en que se estén escurriendo.

En ella habrá guardado siempre un delantal limpio de repuesto o un juego de ropa de los indicados en el artículo 66 por cada persona de las que intervengan en las operaciones que se efectúen en el local de manipulaciones.

ART. 66. Las personas ocupadas en las operaciones que se efectúan en el local de manipulaciones deberán usar delantal largo o pantalones y saco o blusa limpios, blancos y lavables.

ART. 67. En el local de manipulaciones, si él no está anexo a algún otro establecimiento de lechería del mismo propietario, donde ya se tenga el libro de que se trata en seguida, deberá haber un libro foliado, sellado por la Administración Sanitaria, en que los inspectores de la misma dejarán constancia de sus inspecciones y de las observaciones, instrucciones, avisos, etc., que hagan o den a su propietario.

En las usinas o fábricas de lechería también deberá tenerse el libro de que aquí se trata.

ART. 68. Las disposiciones del presente capítulo comprenden también a las usinas y fábricas de lechería, las que deberán darles cumplimiento en cuanto les sean aplicables, bajo pena de cincuenta a cien pesos de multa, según la gravedad de la falta.

ART. 69. Los infractores de los artículos 61, 62, 63, 64, 65, 66 o 67, incurrirán en multa de cinco a cincuenta pesos, según la gravedad de la falta.

No se otorgarán por la Administración Sanitaria los permisos correspondientes, sin comprobar primero si el interesado dispone de todos los elementos necesarios para cumplir lo dispuesto en este capítulo.

CAPÍTULO VI. VENTA DE LECHE EN PUESTOS FIJOS—LECHERÍAS.

ART. 70. Considérase lechería todo puesto fijo de venta de leche al detalle al público consumidor, adonde éste va a buscar la leche que compra.

ART. 71. Dichos establecimientos deberán tener en el frente un letrero que diga "lechería," y este letrero no podrá ser usado por establecimientos donde no se venda leche en las condiciones indicadas en el artículo precedente.

ART. 72. Las lecherías constarán por lo menos del local de que se trata en el capítulo V y del local de venta o despacho al público.

ART. 73. El local de despacho deberá estar al frente, es decir, dar a la calle, y tener por lo menos una puerta a la misma, que permita el acceso inmediato y directo del público que va a comprar leche.

Estará en comunicación directa con la pieza donde se deposite y prepare la leche (la indicada en el art. 64), pero no con la destinada a la limpieza (la indicada en el art. 65).

En cuanto a su construcción, disposición, utensilios y mantenimiento, deberá satisfacer los requisitos indicados en los artículos 62 y 63, salvo las condiciones 5ª, 6ª, 7ª, 8ª, 15ª y 19ª de este último artículo, y con la diferencia de que la pintura podrá no ser blanca, bastando que sea de color claro, y de que la chapa del mostrador deberá ser blanca o de color claro.

ART. 74. En las lecherías, la leche de primera calidad y la de segunda calidad podrán venderse sueltas al consumidor, es decir, serle entregados en los recipientes que lleve a ese efecto.

ART. 75. La leche en despacho deberá estar en depósitos o tanques sin canilla, provistos de tapa que recubra la abertura superior, sus bordes y el cuello del recipiente, y colocados en aparatos refrigeradores, heladeras o cubas con hielo, si la temperatura ambiente es superior a la que debe tener la leche según su calidad.

ART. 76. Los tanques o depósitos mencionados en el artículo precedente se hallarán a la vista del público y de modo que los clientes puedan leer los letreros de que se trata en seguida.

Los que contengan leche de primera calidad llevarán el siguiente letrero, en la forma, lugar y demás condiciones indicadas en el artículo 51:

Leche de primera calidad.
Los niños y enfermos deben consumirla hervida.

Los que contengan leche de segunda calidad llevarán de igual manera este letrero:

Leche de segunda calidad.
Consúmase hervida.

Si la leche es pasteurizada, el primer renglón de esos letreros dirá como sigue: "Leche de primera calidad pasteurizada" o "Leche de segunda calidad pasteurizada," según se trate de una u otra calidad de leche.

Si los recipientes están guardados, encerrados o cubiertos, de tal modo que no se vean sus letreros, éstos deberán ir, en la forma ya indicada, sobre la pared de la heladera cuba, etc., donde los recipientes se hallen colocados. Pero éstos llevarán siempre los letreros susodichos, aunque estén guardados, encerrados o cubiertos.

ART. 77. La leche deberá extraerse de esos depósitos o tanques por su abertura superior, a la vista del cliente, por medio de una medida provista de mango largo, a manera de cucharón, y después de remover bien el líquido con la misma, a fin de que todos la reciban con igual cantidad de gordura.

ART. 78. Cada tanque o depósito estará provisto de su medida especial y ésta deberá permanecer continuamente dentro del depósito respectivo, colocada de tal modo que la parte del mango por donde se toma para usarla no esté sumergida en la leche.

ART. 79. El depósito y su correspondiente medida serán limpiados por lo menos cada veinticuatro horas y además toda vez que se vaya a echar en el primero leche de otra partida (art. 15).

ART. 80. Al lado de cada tanque o depósito habrá un soporte o una percha para poner o colgar en él la tapa del mismo durante las operaciones de echar o extraer leche. La tapa se colocará en ellos boca abajo siempre.

ART. 81. Los depósitos destinados a la leche de primera calidad no serán nunca usados con la leche de segunda calidad, ni los destinados a esta última con la de primera calidad.

ART. 82. La Administración Sanitaria podrá permitir que la leche en despacho se tenga en recipientes con canilla, siempre que el interesado disponga de los elementos de limpieza y esterilización necesarios para mantenerlos en perfectas condiciones de higiene y que a la vez esos recipientes satisfagan los requisitos ya establecidos en esta ordenanza y además los siguientes:

1°. La canilla deberá ser de constitución simple, sin rosca y fácilmente desmontable.

2°. El recipiente deberá estar dispuesto de tal modo que no se pueda extraer la leche por la canilla, sin que el líquido sea agitado de tiempo en tiempo.

3°. El mecanismo para agitar la leche deberá ser tal que no haya ninguna pieza que se mueva en el interior del recipiente ni en contacto con el líquido.

Para usar esta clase de recipientes los interesados deberán solicitar en cada caso una autorización especial de la Administración Sanitaria.

ART. 83. Debajo de cuanto letrero se coloque en las lecherías, relativo a la leche que venden, deberá ponerse siempre el aviso ya indicado sobre la forma en que debe ser consumido el producto, en letras de igual tamaño y color.

ART. 84. En las lecherías que tengan mesas para servir leche o sus derivados o preparados a clientes que vayan a consumirlos allí mismo, el lugar donde se hallen las mesas estará separado por medio de una baranda por lo menos del despacho de leche al público que la compra para llevársela, de modo que los clientes que concurren a las mesas se hallen a una distancia de tres metros cuando menos del mostrador y de los depósitos de que se trata en el artículo 75 y siguientes.

El acceso al lugar de despacho sólo se permitirá a las personas que vayan a comprar leche para llevársela.

ART. 85. En las lecherías, además de la venta de leche, sólo se permitirá la de huevos frescos, quesos frescos y sin olor pronunciado, crema, manteca, cuajadas y productos análogos derivados de la leche, miel y otros productos de granja conservados y vendidos en envases cerrados en el lugar de producción, todo lo cual deberá depositarse y tenerse en condiciones que no atraigan las moscas y no puedan comunicarle olores extraños a la leche.

También podrán tenerse y venderse masas secas y pan para ser consumidos en las mesas del local.

Pero ni los quesos, ni ninguno de los productos no derivados de la leche podrán ser tenidos ni vendidos en las lecherías en cantidades tales que hagan perder a estos establecimientos su verdadero carácter o que influencien en lo más mínimo el cuidado y las condiciones de la leche.

ART. 86. Toda lechería anexa a una chocolatería, confitería, restaurant o cualquier otro negocio deberá estar completamente separada de él, y las puertas que la pongan en comunicación con él deberán ser de cierre automático y abrirse únicamente para pasar.

ART. 87. Las personas que atiendan el despacho usarán camisa blanca y corbata e indumentaria exterior como la indicada en el artículo 66.

ART. 88. En toda lechería se llevará un libro como el indicado en el artículo 67.

ART. 89. El permiso que otorgue la Administración Sanitaria a las lecherías deberá hallarse en el local de despacho, a la vista del público, en un cuadro con vidrio.

ART. 90. No se otorgarán por la administración sanitaria los permisos correspondientes, sin cerciorarse primero de si el interesado dispone de los elementos necesarios para satisfacer las prescripciones contenidas en este capítulo.

La Administración Sanitaria podrá prohibir la venta de leches de primera calidad certificada o de primera calidad a las lecherías que por su mal mantenimiento u otras causas no ofrezcan garantías suficientes de entregar esas leches al consumidor en las condiciones exigidas en esta ordenanza.

Los infractores de los artículos 71, 84, u 86 incurrirán en cincuenta pesos de multa. Se les clausurará el establecimiento, si después del segundo aviso y de vencido el plazo que les señale la administración sanitaria, no se colocan en las condiciones exigidas.

Los de los artículos 73, 80, 85, 87, 88, u 89 incurrirán en multa de cinco a cincuenta pesos, según la gravedad de la falta.

Los de los artículos 75, 77, o 78, en multa de treinta pesos, si se trata de leche de primera calidad, y de quince pesos, si de segunda calidad.

Los de los artículos 76 u 83, en multa de cincuenta pesos la primera vez, de cien pesos la segunda y retiro definitivo del permiso para intervenir en cualquier forma en el comercio de lechería la tercera. En los casos de infracción del artículo 76, además de la multa, la leche caerá en comiso.

Los del artículo 79, en multa de treinta pesos, si se trata de leche de primera calidad, y de quince pesos, si de segunda calidad. La leche puesta en el depósito que no haya sido limpiado previamente será decomisada.

Los del artículo 81, en multa de cincuenta pesos y comiso de la leche que se halle en el depósito o tanque destinado a leche de otra calidad.

CAPÍTULO VII. VENTA DE LECHE A DOMICILIO; VENDEDORES AMBULANTES; REPARTIDORES; CARROS Y DEMÁS VEHÍCULOS DE REPARTO.

ART. 91. Bajo pena de cien pesos de multa y comiso de la leche que transporte, no se usará ningún carro o vehículo para el transporte o venta de leche a domicilio que no haya sido previamente aprobado y registrado por la Administración Sanitaria. El carro o vehículo que circule en la vía pública, sin estar aprobado y registrado, será detenido hasta que el interesado abone la multa susodicha, corriendo por su cuenta los gastos de depósito, y sin responsabilidad para la administración sanitaria por los deterioros que pueda sufrir durante su detención.

Los carros y demás vehículos de reparto o venta de leche a domicilio serán con elásticos, completamente cerrados, con paredes, piso y techo aisladores, revestidos interiormente de chapa metálica inoxidable y bien unida, y estarán provistos de depósitos para hielo y para el agua de descongelación, de manera que la leche pueda mantenerse en ellos a la temperatura que corresponda según las prescripciones de la presente ordenanza y que no se acumule agua en el interior del vehículo. Estarán totalmente pintados de blanco, salvo las ruedas, que podrán ser pintadas de cualquier otro color. La pintura será impermeable.

Esos vehículos serán de limpieza y desinfección fáciles y deberán mantenerse siempre en buen estado de conservación y aseo, interior y exteriormente.

Si las canillas de los tanques de la leche salen al exterior del vehículo, estarán provistas de una cubierta especial, convenientemente dispuesta para excluir toda causa de contaminación.

Los vehículos podrán ser de tracción humana, animal o mecánica.

ART. 92. Los vehículos llevarán pintado, en negro y en caracteres de molde, en una de las paredes laterales o en la posterior, el número de su registro en la administración sanitaria, precedido de las iniciales A. S., el nombre de la empresa, firma o persona por cuenta de quien se vende la leche que transportan, la dirección del respectivo establecimiento o del domicilio del vendedor, si no tiene establecimiento alguno, y un letrero indicativo de la calidad de la leche o de las leches que transportan y de la manera cómo deben ser consumidas.

Para la leche de primera calidad certificada, este último letrero será tal como se indica en el artículo 42, suprimiendo el renglón 5°. Para las leches de primera calidad y de segunda calidad, tal como se indica en los artículos 46, y 52, respectivamente.

El número de registro y las iniciales que lo preceden, así como los renglones donde se indica en los letreros la calidad de la leche y la manera cómo debe ser consumida, serán en letras de ocho centímetros de altura por uno y medio de grueso, por lo menos, y todo el resto de lo que debe ir escrito sobre el carro, en letras de cinco centímetros de grueso, cuando menos.

La leche vendida, ofrecida en venta o presentada para la venta como de una calidad que no esté indicada o anunciada en el exterior del vehículo en la forma establecida,

caerá en comiso, y el infractor incurrirá en multa de cincuenta pesos la primera vez, cien pesos la segunda y retiro definitivo del permiso para intervenir en cualquier forma en el comercio de lechería la tercera.

Siempre que no se trate de maniobras de mala fe, que tienen penas especialmente establecidas, las demás infracciones del presente artículo serán penadas con multa de cincuenta pesos.

En los casos de que se trata en los dos párrafos precedentes, el vehículo será detenido, en las condiciones establecidas en el artículo 91, hasta tanto se abone la multa impuesta.

ART. 93. Se prohibe llevar en el pescante recipientes de cualquier clase, sin leche o con leche, comprendido el jarro usado como medida, que tampoco se llevará colgado de la cintura, bajo pena de diez pesos de multa en todos los casos y detención del vehículo, en las condiciones ya establecidas, hasta tanto se abone la multa.

Recipientes y medida irán siempre guardados en el interior del vehículo.

ART. 94. En los vehículos de reparto no se llevará agua ni ninguna otras sustancia o cosa más que leche, crema, manteca y otros derivados de la leche, siempre que satisfagan éstos las condiciones indicadas en el artículo 85, y los recipientes a ellos destinados.

Se prohibe también llevar en ellos, perros o cualquier otro animal y usarlos para otro destino que para el transporte de la leche, aún fuera de las horas de reparto.

A los infractores de este artículo se les aplicará una multa de cinco a cincuenta pesos, según la gravedad de la falta, para apreciar la cual se tendrá en cuenta la calidad de la leche que transporten en el vehículo, y se les detendrá éste, si se halla en la vía pública, en la forma y por el término indicados en el artículo precedente.

ART. 95. Se prohibe trasvasar la leche de los recipientes en que se transporta a otros, con objeto de bajarla o sacarla del vehículo en estos últimos y echarla de aquí en el recipiente del consumidor, bajo las penas establecidas en el artículo 93.

La leche que se venda o reparta suelta, deberá ser echada directamente del tanque o tarro en que se transporte a la medida y de aquí al recipiente del consumidor.

ART. 96. Los repartidores y los vendedores ambulantes de leche usarán la indumentaria exterior indicada en el artículo 66, bajo las penas establecidas para los infractores de este artículo.

ART. 97. Todo repartidor, por su cuenta o por la de otro, llevará siempre consigo una libreta numerada que lo acreditará como tal, expedida por la Administración Sanitaria, mediante el pago de su costo. Esta libreta llevará el retrato del repartidor y el texto de la presente ordenanza y además constarán en ella los siguientes datos: nombre de la persona, empresa o firma por cuenta de quien se hace el reparto y dirección del respectivo establecimiento, nombre y apellido del repartidor, ubicación de su establecimiento, o, si no tiene ninguno, de su domicilio, nacionalidad y edad del repartidor, número del permiso del establecimiento respectivo y número de registro del carro que usa el reparticor. La libreta tendrá veinte páginas en blanco, donde los inspectores de la Administración Sanitaria anotarán los avisos y observaciones hechas al repartidor y las infracciones cometidas por éste, con indicación de causas y de fecha.

Al repartidor que no lleve consigo la libreta durante el reparto se le aplicará una multa de 15 pesos las tres primeras veces y de 50 las sucesivas y se le detendrá siempre el carro, en las condiciones ya establecidas, hasta que la presente y abone la multa impuesta.

ART. 98. A los lecheros ambulantes o repartidores que por el deficiente mantenimiento del vehículo u otras causas no ofrezcan suficientes garantías de entregar al consumidor la leche de primera calidad certificada o la leche de primera calidad en las condiciones exigidas en esta ordenanza, la administración sanitaria podrá prohibirles vender o repartir esas clases de leches, so pena de decomisárselas, aplicarles una multa de cien pesos y detenerles el vehículo en las condiciones y por el término indicados en el artículo precedente.

CAPÍTULO VIII. PERSONAS QUE INTERVIENEN EN EL COMERCIO DE LECHERÍA, EN GENERAL.

ART. 99. Del reparto, venta y manipulación de la leche no se ocupará ninguna persona afectada de enfermedades contagiosas que puedan trasmitirse por intermedio de la leche, o de llagas supurantes, úlceras, erupciones o eczemas supurantes o húmedos de los brazos, manos o cara, ni que lleve vendajes en estas mismas partes.

ART. 100. Toda persona ocupada en el reparto, venta o manipulación de la leche estará provista de un certificado médico expedido por la administración sanitaria y que deberá ser renovado anualmente, bajo pena de cincuenta pesos de multa.

ART. 101. Las personas de que se trata en los precedentes artículos deben mantenerse siempre aseados y, en particular, cuidarán de tener sus manos limpias.

CAPÍTULO IX. PRODUCCIÓN DE LA LECHE DE PRIMERA CALIDAD CERTIFICADA.

1. VACAS PRODUCTORAS; SUS CONDICIONES Y ESTADO SANITARIO.

ART. 102. El lote productor de leche de primera calidad certificada constará de cuatro vacas cuando menos. La edad de los animales no pasará de doce años.

ART. 103. Las vacas destinadas a producir esa leche serán examinadas individualmente y tuberculinizadas por un veterinario de la administración sanitaria antes de entrar a formar parte del lote productor.

Después, serán examinadas por el mismo por lo menos una vez al mes y tuberculinizadas cuantes veces él lo considere necesario para descartar cualquier sospecha de tuberculosis.

La tuberculinización se repetirá por lo menos cada año.

ART. 104. Las vacas que reaccionen como tuberculosas a la inoculación de tuberculina o que presenten signos clínicos de tuberculosis serán marcadas a fuego con una T en el tercio superior de la tabla izquierda del cuello. Las que den reacción dudosa, con una D, en la misma forma y lugar. Unas y otras serán immediatamente separadas y aisladas, y sacadas del establecimiento dentro de un plazo de 48 horas. Aunque dejaran de reaccionar en lo sucesivo, no podrán nunca formar parte del lote productor ni volver al establecimiento.

Las que al examen clínico o bacteriológico resulten afectadas de cualquier enfermedad serán inmediatamente separadas y aisladas, hasta que el veterinario oficial las considere sanas o declare que su leche no ofrece inconveniente ni peligro alguno Entre tanto, su leche no será utilizada. Si considera que ellas deben ser definitivamente eliminadas del lote productor, serán sacadas del establecimiento en el plazo de 48 horas.

Se prohibe expresamente utilizar para la producción de leche de primera calidad certificada, o tener dentro de los establecimientos que la producen, vacas que no tengan sus cuatro mamas íntegras y en capacidad de funcionar plenamente, como también dedicar a la producción de tal leche o tener dentro del lote productor vacas afectadas de cualquier trastorno digestivo acompañado de diarrea.

ART. 105. Las vacas que formen el lote productor serán señaladas con un broche numerado que se les aplicará en la oreja.

Con ellas no se colocará nunca, en el establo, ni en los potreros, ni en parte alguna, ninguna vaca que no haya sido antes tuberculinizada y examinada por el veterinario oficial y declarada sana por él. Tampoco podrán estar con ellas animales de otras especies o vacas destinadas a producir leche de otra calidad.

ART. 106. Quince días antes de parir, las vacas serán separadas del lote productor, colocadas en establos o potreros especiales y mantenidas aquí hasta después de ocho días de la parición. Durante el tiempo de separación, su leche no será utilizada. Pasado este plazo, y previo examen del veterinario oficial, podrán volver al lote productor, pero sin su ternero, que desde ese momento no tocará más a la madre ni estará a su lado.

ART. 107. De todo trastorno de la salud o novedad notados en las vacas se dará aviso inmediato a la administración sanitaria, que dispondrá en seguida su visita por un veterinario. Entre tanto, desde el primer momento, el animal será retirado del lote productor y su leche no será utilizada hasta que el veterinario oficial lo ordene.

ART. 108. A efectos de dar cumplimiento a lo dispuesto en los artículos anteriores, en todo establecimiento dedicado a la producción de leche de primera calidad certificada habrá potreros o establos especiales para el lote productor, para los animales destinados a formar parte de él y aún no examinados, para los afectados o los sospechosos de tuberculosis o que por cualquier otra causa haya que retirar definitivamente del lote productor y, finalmente, para colocar la vacas durante el período de la parición.

Los abrevaderos de esos potreros no serán comunes ni próximos, debiendo hallarse, cuando sea posible, a distancia de por lo menos cien metros unos de otros.

Las personas dedicadas al cuidado y ordeño de las vacas del lote productor o que manejen su leche no atenderán los animales reaccionantes o sospechosos de tuberculosis, y sólo podrán hacerlo con los otros cuando el veterinario oficial lo permita.

ART. 109. La administración sanitaria hará examinar desde el punto de vista químico y bacteriológico una vez al mes por lo menos, muestras colectivas de leche del lote productor, recogidas con las garantías necesarias. Esas muestras se recogerán de la mezcla de la leche de cincuenta vacas cuando más.

En caso de comprobarse en esas muestras agentes infecciosos que puedan proceder de las vacas, se harán las investigaciones clínicas y bacteriológicas individuales necesarias para descubrir el animal infectante.

Cuando la administración sanitaria o el veterinario oficial lo estimen conveniente, podrán recogerse muestras colectivas o individuales de leche, de productos patológicos, de forrajes, aguas y, en general, de todo lo que se requiera para asegurarse del buen estado sanitario de los animales y de las condiciones de la leche.

ART. 110. Los interesados podrán hacer asistir sus animales por el veterinario particular que estimen conveniente, pero el veterinario oficial deberá ser enterado siempre del tratamiento a que se los someta.

Los animales enfermos no serán tratados por ninguna persona que no tenga el título de médico veterinario. Ni aun medicamentos caseros (sulfato de soda, etc.) podrán administrárseles sin la intervención del veterinario.

ART. 111. Las vacas del lote productor no serán tratadas con medicamentos de acción enérgica o capaces de pasar a la leche. Se prohibe especialmente administrarles áloe, ársenico, emético (tártaro estibiado), arcolina, heléboro blanco, preparados mercuriales, yodo, eserina, pilocarpina, estricnina y otros alcaloides. La leche de las vacas tratadas con estos medicamentos no podrá ser utilizada hasta pasados cuatro días de cesado el tratamiento.

ART. 112. Cuando la Administración Sanitaria lo considere necesario podrá exigir que las vacas sean vacunadas o sometidas a tratamientos preventivos contra determinadas enfermedades que las amenacen.

ART. 113. En los establecimientos productores de leche de primera calidad certificada se llevará un libro dispuesto en la forma que indique la administración sanitaria, donde se anotará respecto de cada vaca el número que tenga, su reseña (raza, edad, pelaje, señas particulares, señales, marcas, etc.), la fecha del primer examen del veterinario oficial y su resultado, fecha de instalación en el lote productor, fechas en que fué servida y de la parición, las exclusiones temporarias del lote productor, con indicación de fechas, duración y motivos, y las visitas sucesivas a que haya sido sometida por el veterinario oficial, con indicación de fechas, resultados y prescripciones u observaciones a que haya habido lugar.

Este libro estará siempre a disposición del veterinario inspector.

ART. 114. En esos establecimientos, por lo menos dos veces por semana se medirá la cantidad de leche que dé en el día cada vaca y se registrará el dato en un libro especial, que estará siempre a disposición del veterinario inspector. Las anotaciones serán conservadas durante seis meses.

2. ALIMENTACIÓN DE LAS VACAS PRODUCTORAS DE LECHE DE PRIMERA CALIDAD CERTIFICADA.

ART. 115. Los potreros o cuadros donde se alimenten las vacas a pastoreo serán altos, libres de pantanos o charcos y de todo otro depósito de aguas contaminadas o no potables, no inundables por las aguas superficiales ni subterráneas y provistos de buenos pastos naturales o artificiales.

En ellos, ni a una distancia de cien metros de ellos, no habrá chiqueros, estercoleros, ni otras habitaciones de animales, depósitos de residuos o establecimientos que despidan malos olores.

Tampoco habrá en ellos, ni a cien metros de ellos, cadáveres de animales, carroñas, huesos u otros restos de animales muertos.

Además, la ubicación de esos potreros será tal que los animales no estén en ningún caso obligados a transitar a distancia menor de cien metros de esas habitaciones, depósitos, establecimientos y restos.

ART. 116. Además de la alimentación a pastoreo podrá administrarse a las vacas los siguientes forrajes:

(a) Heno (pasto seco) de buena calidad, bien cosechado, de color fresco y olor aromático, libre de plantas tóxicas, mohos (no será ardido) y polvo.

(b) Paja de cereales de la misma calidad y estado.

(c) Afrecho de centeno y de trigo.

(d) Avena, cebada, centeno y maíz, molidos, rotos o aplastados.

(e) Harina de semilla de lino.

Los granos y harinas serán de buena calidad y en buen estado de conservación.

Quien desee administrar otro forrajes pedirá previamente autorización a la administración sanitaria.

No se permitirá en ningún caso que los animales consuman forrajes capaces de producir diarrea u otros trastornos, de comunicar a la leche olor o gusto extraños o de disminuir su calidad.

ART. 117. El agua de bebida de los animales, así como toda el agua usada con cualquier fin en los establecimientos productores de leche de primera calidad certificada, debe haber sido reconocida potable por la Administración Sanitaria.

Cada potrero tendrá su abrevadero especial, separado de los que pertenecen a los potreros vecinos.

En los abrevaderos no se lavará ropa, ni las manos, ni recipiente alguno, ni se cumplirá ningún fin doméstico, ni otros, capaces de ensuciar o contaminar el agua.

Se hallarán siempre limpios y provistos de agua limpia y fresca.

Estarán emplazados en lugares altos y de tal modo que alrededor de ellos no se formen charcos o barro, donde los animales puedan echarse. También se evitará que junto a ellos o a su alrededor se acumule el estiércol de los mismos animales.

ART. 119. No se permitirán los cambios bruscos de régimen alimenticio.

El pasaje del régimen seco al de pasto verde, e inversamente, será gradual.

En la época de los pastos tiernos, si éstos ocasionan diarrea, los animales mantenidos a pastoreo recibirán un suplemento de pasto seco, a fin de evitar ese inconveniente. Lo mismo, se adoptará igual procedimiento, si la alimentación exclusiva con pasto verde de cualquier clase produce ese trastorno.

ART. 119. En todo establecimiento de los indicados habrá un local especialmente destinado al depósito y conservación de los forrajes, de dimensiones proporcionadas a las necesidades, bien ventilado, seco, limpio y emplazado en un lugar alto.

3. CAMPO Y ESTABLOS DE LAS VACAS PRODUCTORAS DE LECHE DE PRIMERA CALIDAD CERTIFICADA.

ART. 120. Los animales podrán ser tenidos en establos todo el año o en ciertas épocas de él, pero se les dará siempre, salvo que el mal tiempo no lo permita, por lo menos cinco horas diarias de soltura al aire libre, en potreros como los indicados en el artículo 115.

ART. 121. Cuando los animales sean mantenidos continuamente a campo y no haya establos para ellos, habrá en cada potrero por lo menos un tinglado o cobertizo de dos aguas, de dimensiones proporcionadas al número de vacas que haya en el potrero, con tabique mediano, piso impermeable y fácil de limpiar, y orientado y dispuesto de tal modo que los animales puedan protegerse en él de las lluvias y del viento.

Se evitará que en él, y sus alrededores se acumulen deyecciones o el agua de las lluvias, o se formen baches, a fin de que los animales, en lo posible, no se ensucien, sobre todo al echarse.

ART. 122. Los establos se hallarán emplazados sobre un terreno alto. Sus pisos serán de cemento en toda su extensión o de material análogo, impermeable, y tendrán una inclinación que permita la corriente de los líquidos hacia bocas de desagüe cubiertos con rejilla y en conexión con el sistema de drenaje. La superficie del piso se hallará a 20 centímetros por lo menos sobre el nivel del suelo que rodea el establo.

En cuanto a lo demás, los establos deberán satisfacer las condiciones indicadas en los artículos siguientes.

ART. 123. El sistema de drenaje terminará en pozos adecuadamente construidos y estará dispuesto de tal modo que sus emanaciones no refluyan al establo.

ART. 124. Las paredes del establo, hasta dos metros de altura por lo menos, serán de material (obra de fábrica) y revestidas de cemento impermeable y liso o de baldosas o azulejos, con las junturas bien tomadas con cemento.

Los ángulos formados por las paredes entre sí, hasta esa altura, y por ellos y el piso serán redondeados, para facilitar la limpieza.

ART. 125. El resto de las paredes y los cielo rasos podrán ser de madera cepillada. Si son de material (obra de fábrica), tendrán su superficie lisa. En todos los casos, salvo que se hallen revestidos de material impermeable, estarán pintados con lechada de cal o alguna pintura impermeable de color claro.

ART. 126. En la construcción del establo no habrá nada de madera más que lo indicado en el artículo precedente y las puertas y ventanas. Los parantes o columnas de sostén interiores, los tabiques de separación de los animales, las rejillas para el pasto, comederos, bebederos, etc., serán de hierro, cemento armado o material, impermeables, con sus superficies lisas y sus aristas y bordes redondeados.

ART. 127. El establo tendrá suficientes dimensiones como para que cada vaca disponga de treinta metros cúbicos de espacio libre, cuando menos.

El cielo-raso se hallará en sus partes más bajas a 5 metros por lo menos de altura sobre la superficie del piso.

ART. 128. La orientación, construcción, disposición y ventilación del establo serán tales que el aire interior se mantenga fresco, seco y agradable y que no haya corrientes de aire en el recinto.

La temperatura del establo se mantendrá entre 16 y 18 grados.

Las ventanas serán de dimensiones y en número suficientes para que haya por lo menos 12,600 centímetros cuadrados de abertura por cada 30 metros cúbicos de espacio libre interior. Estarán situadas en forma que la luz se distribuya abundante y uniformemente en todo el establo y se abrirán hacia adentro, sobre eje horizontal inferior, de suerte que al entrar el aire vaya hacia arriba.

El establo estará provisto de ventiladores de tiraje interceptables a voluntad, en número y con dimensiones suficientes para que por cada 30 metros cúbicos de espacio libre interior haya por lo menos 375 centímetros cuadrados de abertura de ventilación.

ART. 129. La disposición interna del establo será del tipo o modelo llamado holandés, en lo que se refiere a la forma como serán tenidos los animales.

La superficie ocupada por cada vaca será pequeña. Tendrá una longitud tal que los excrementos caigan naturalmente en la canaleta de deyecciones que correrá detrás de los pies posteriores de los animales. Su ancho será también reducido, de modo que quede espacio para los pies cuando las bestias se acuesten, pero que sea imposible a éstas ladearse y alejar los cuartos traseros de la susodicha canaleta.

Las canaletas de deyecciones tendrán dieciséis centímetros por lo menos de profundidad en todas sus partes, serán construidas de cemento u otro de los materiales indicados para el piso del establo y adecuadamente inclinadas y drenadas.

Los comederos y bebederos serán bajos, de modo que los animales, al echarse, puedan extender su cuello y cabeza por encima de ellos. Su fondo no estará a más de 15 centímetros sobre la superficie del piso circundante.

ART. 130. En los establos dispuestos de tal manera que las vacas estén opuestas por sus partes posteriores habrá un espacio por lo menos de 2.50 metros entre los bordes exteriores de las canaletas de deyecciones opuestas.

El establo estará provisto de pasillos para servir los alimentos a los animales sin tener necesidad de pasar por entre ellos ni molestarlos.

Los pasillos y caminos y todos los espacios que se hallen detrás de las vacas serán por lo menos tan altos como los lugares ocupados por ellas.

ART. 131. Será preferible que cada vaca tenga su comedero y bebedero aparte. Estos serán metálicos o de otro material impermeable, inoxidables y de fácil limpieza.

ART. 132. Todo establo tendrá su servicio de agua corriente convenientemente dispuesto y que baste para todos los propósitos.

Si las vacas son ordeñadas en el establo, en un lugar adecuado de éste o en conexión con él habrá un servicio de agua caliente con todo lo necesario para lavarse las manos (pileta o gran palangana, jabón, cepillo y toallas o lienzos limpios).

ART. 133. Se tratará por todos los medios posibles de que el establo esté siempre libre de moscas.

Puertas y ventanas estarán provistas de tela metálica, a fin de impedir su entrada.

ART. 134. Todo el establo estará construido, dispuesto y mantenido de tal modo que la limpieza y desinfección sean fáciles.

Los establos se hallarán siempre limpios, libres de tierra, polvo y telarañas.

Si las paredes y cielo-raso son blanqueados con cal, el blanqueo se repetirá cada seis meses por lo menos, previo raspaje del antiguo.

Los excrementos serán retirados tan frecuentemente como sea necesario para evitar en lo posible la producción de malos olores y que las vacas se ensucien. Por lo menos serán sacados dos veces por día.

Diariamente se hará una limpieza completa del establo.

Los pilones o recipientes donde se sirven los alimentos a los animales se limpiarán después de cada comida.

Cada cinco días por lo menos, el piso de todo el establo, comprendidos los lugares donde se hallan las vacas y las canaletas de deyecciones, las paredes hasta la altura de 2 metros y todo lo que esté dentro de la misma altura, serán lavados a fondo, a cepillo y con abundante agua.

En los establos no habrá deshechos, basuras, ni nada que no sea necesario para su buen mantenimiento o para el cuidado de los animales.

ART. 135. Si el establo es de madera en sus partes superiores, sobre él no habrá depósitos de forrajes, ni instalaciones de ninguna especie.

Ninguna parte del establo será usada como habitación de personas para dormir, ni para ningún otro fin doméstico.

El establo tampoco se hallará en comunicación con habitaciones ni piezas de fines domésticos, ni con caballerizas u otras habitaciones de animales.

ART. 136. Los excrementos de los animales serán depositados a distancia de cien metros por lo menos del establo, en dirección contraria a los vientos predominantes y en condiciones de impedir en lo posible el desarrollo y acumulación de las moscas y la producción de malos olores.

ART. 137. El terreno que rodea el establo estará nivelado de tal modo que no se acumulen en él aguas superficiales y será mantenido limpio, seco y libre de residuos, basuras, trastos viejos o cualesquiera otros inconvenientes.

Delante de las puertas habrá un veredón de cuatro metros de fondo y dos metros más ancho que la puerta correspondiente, por lo menos, construído de material sólido, liso e impermeable.

En un radio de cien metros del establo no habrá aguas estancadas, pantanos, barriales, sumideros o depósitos de estiércol, ni porquerizas.

ART. 138. No habrá letrinas a distancia menor de veinte metros del establo.

Todas las letrinas del establecimiento serán cerradas, de material, con revestimiento interior impermeable hasta dos metros de altura, protegidas contra el acceso de las moscas, con los asientos provistos de tapa y con servicio de agua corriente. Siempre estarán limpias, en condiciones higiénicas.

4. LIMPIEZA DE LAS VACAS PRODUCTORAS DE LECHE DE PRIMERA CALIDAD CERTIFICADA.

ART. 139. Todo el establecimiento productor de leche de primera calidad certificada estará dispuesto y mantenido de tal modo que las vacas se expongan lo menos posible a ensuciarse.

ART. 140. Cuando se use cama para los animales, ellas serán de paja de cereales o de pasto, limpios, sin tierra o polvo, ni mohos, ni mal olor. Se prohibe utilizar con tales fines paja u otras materias usadas en camas de personas o en embalajes o en cosas análogas.

ART. 141. Las vacas estarán siempre limpias, sin caspa, ni barro, ni estiércol pegados a su piel. Se les podrá pasar la mano por encima sin ensuciársela.

El pelo de los ijares, del vientre alrededor de la ubre, de la ubre, del muslo y parte superior de la pierna y el de la cola serán mantenidos cortos.

Las vacas serán completa y prolijamente limpiadas a cepillo una vez al día. Las partes sucias de estiércol, barro, etc., que no puedan ser limpiadas a seco, se lavarán con agua y jabón.

ART. 142. Para la limpieza a seco y lavado de las vacas mantenidas continuamente a campo se tendrá un tinglado especial, con piso impermeable, drenaje adecuado y provisión de agua corriente.

En cuanto al emplazamiento de ese tinglado y su orientación y situación respecto de otros lugares, instalaciones o locales, su mantenimiento, limpieza y usos, deberán satisfacerse las condiciones de un establo, en la medida que le sean aplicables. Estará ubicado y dis puesto de tal modo que el viento no pueda llevar hacia otros locales (lechería, etc.) los pelos y el polvo que se desprendan de los animales al limpiarlos. Podrá estar próximo al local de ordeño, pero no en directa comunicación con él.

Cuando se tengan las vacas en establos, su limpieza podrá hacerse en ellos; pero se considerará en mejores condiciones higiénicas el establecimiento que, teniendo establo, disponga también de un local especial para ese objeto, anexo a aquél.

5. ORDEÑO DE LA LECHE DE PRIMERA CALIDAD CERTIFICADA.

ART. 143. Esta operación se efectuará con el máximum de limpieza que sea dado y de manera que la leche se contamine lo menos posible con microbios del exterior.

ART. 144. Se hará en el establo o en un local especialmente destinado a ese objeto Este último existirá siempre en el establecimiento y en él deberá efectuarse siempre el ordeño, si las vacas son continuamente mantenidas a campo (si no hay establo).

El local de ordeño será muy abundantemente ventilado, seco y con mucha luz. En cuanto a emplazamiento, estado y mantenimiento del terreno circundante, ubicación respecto de otras instalaciones, orientación, naturaleza del piso, paredes y cielo-raso, temperatura interior, servicio de agua, drenaje, conservación, limpieza, defensa contra las mocas, usos, etc., deberá llenar las condiciones indicadas para el establo, en la medida que le sean aplicables, con la salvedad de que la ventilación y la luz tendrán que ser por lo menos el triple que las del establo. Sus dimensiones estarán en relación con el número de vacas que se ordeñen a la vez y serán tales que permitan la ope-

ración del ordeño con holgura. En él habrá un servicio para lavarse las manos como el indicado en el artículo 132.

Él será ocupado por las vacas únicamente en el momento en que van a ser ordeñadas. En seguida será limpiado a fondo.

Habiendo buen tiempo, sus puertas, ventanas y ventiladores estarán siempre abiertos durante el día.

En él no deberá hacerse la limpieza general de los animales.

ART. 145. Es indispensable que las vacas permanezcan tranquilas durante el ordeño. A este efecto tendrán que ser animales perfectamente mansos y habituados a la operación y se evitará durante ella todo lo que pueda excitarlos.

ART. 146. Las vacas que en el momento del ordeño se hallen mojadas, por haber estado expuestas a la lluvia o por otras causas, serán perfectamente escurridas antes de comenzar la operación, de tal modo que de su piel no pueda desprenderse ninguna gota líquida. Esa preparación del animal se hará en el local de limpieza (artículo 142) o, si éste no existe, en el establo.

ART. 147. Antes del ordeño se evitará todo lo que pueda ocasionar levantamiento de polvo y desprendimiento de malos olores.

Las limpiezas generales del establo, la distribución de las comidas o forrajes y el cambio y removido de las camas se efectuarán inmediatamente después de terminar un ordeño.

La remoción de excrementos, las limpiezas parciales de las canaletas de los mismos, etc., no se harán tampoco durante la hora que precede a aquella operación.

La limpieza general de las vacas, cuando se haga dentro del establo, será efectuada también en seguida de terminar un ordeño.

Si se trata de animales continuamente mantenidos a campo, su limpieza general se hará inmediatamente antes de comenzar un ordeño, evitando en lo posible los lavados extensos de las partes superiores y posteriores del cuerpo, que se dejarán para después de él.

En todos los casos, cuando sea de estricta necesidad lavar esas partes antes del ordeño, deberán escurrirse bien las regiones mojadas de manera que mientras se efectúa el mismo no puedan desprenderse gotas de líquido capaces de llegar a las manos del ordeñador, la ubre, las tetas o el recipiente donde se recoge la leche. En una palabra, no se ordeñará ninguna vaca cuya piel esté tan mojada que de ella puedan caer gotas de líquido.

Antes de comenzar a ordeñar en el establo, se abrirán puertas y ventanas, a fin de que el aire se renueve y se evacúen los malos olores.

ART. 148. Las vacas serán inmovilizadas durante el ordeño. Sus colas estarán sujetas.

ART. 149. Inmediatamente antes de ordeñar cada vaca, se le limpiará la ubre, las tetas y las partes limítrofes.

Esta limpieza se hará, sea sacando por lo pronto las gruesas porciones de suciedad, lavando después con agua tibia (a temperatura más o menos igual a la del cuerpo del animal) y, finalmente, frotando y secando bien con un lienzo o toalla; sea frotando primero con un paño seco o ligeramente húmedo y en seguida con otro, seco o apenas engrasado. Los trapos, lienzos o toallas serán blancos, de tela suave, lavables y limpios, debiendo a este último efecto haber una buena provisión, para que puedan cambiarse a menudo. La materia grasa que se use será pura y en buen estado de conservación (no rancia), incapaz de irritar la piel.

Será preferible que de esa limpieza se encargue especialmente una persona, para que el ordeñador pueda operar inmediatamente con sus manos limpias.

En caso de volver a ensuciarse durante el ordeño las partes indicadas, antes de proseguir habrá que limpiarlas otra vez.

ART. 150. El ordeñador llevará durante el ordeño sobre-pantalones, blusa larga o delantal de mangas cortas, bien cerrados, y gorro que contenga y recubra los cabellos,

todo de tela blanca y lavable y en perfecto estado de limpieza. Será preferible que en lugar de blusa y sobre-pantalones separados use una combinación de una sola pieza que comprende las dos cosas y especial para esos fines.

Para cada ordeñador habrá siempre disponible, además del que lleven puesto, tres juegos de la ropa susodicha, perfectamente limpios.

ART. 151. El ordeñador cumplirá su tarea con las manos y antebrazos descubiertos y perfectamente limpios.

Antes de empezar a ordeñar se lavará manos y antebrazos con agua tibia, jabón y cepillo, operación que repetirá antes de ordeñar cada vaca, y aún durante el ordeño de cada una, si se le ensucian entonces.

ART. 152. El banquillo del ordeñador será de fácil limpieza y estará limpio siempre.

El ordeñador lo llevará sujeto a su cuerpo, a fin de no tener que tocarlo con sus manos durante el ordeño.

ART. 153. Durante el ordeño, el operador evitará tocar con las manos el cuerpo de la vaca, salvo sus tetas ya limpias, a fin de no ensuciárselas o contaminárselas. Tratará de mantener el animal en posición conveniente sin tocarlo con las manos.

ART. 154. El ordeño se hará a seco (tetas y ubre de la vaca y manos del operador secas durante toda la operación).

Se prohibe expresamente ponerse saliva en las manos, o mojárselas o mojar las tetas con la misma leche de la vaca. Quien haga esto incurrirá en multa de cien pesos, sin perjuicio de exigir, si se estima conveniente, que sea eliminado del personal del establecimiento.

ART. 155. Los tres primeros chorros de leche de cada teta serán recogidos aparte y no serán utilizados en ninguna forma para el consumo de las personas.

ART. 156. Los recipientes en que se ordeñe la leche estarán perfectamente limpios y esterilizados a seco.

Su boca no tendrá nunca más de veinte centímetros de diámetro. Se preferirán los recipientes con embudo y filtro de algodón o con tapa y muy pequeña abertura para la entrada de la leche.

ART. 157. La leche que se haya ensuciado con estiércol o en otra forma cualquiera no se mezclará con la leche limpia ni se contará como leche de primera calidad certificada.

ART. 158. En seguida de ordeñada la leche se echará en un recipiente colector, a través de un filtro que le servirá de tapa.

La leche se retirará prontamente del establo, para evitar en lo posible que se contamine y que tome el olor de los animales o del estiércol. A estos fines, será preferible tener el recipiente colector fuera del establo, en un lugar limpio y protegido del polvo y de las moscas.

Del establo, o del lugar donde se halle el recipiente colector, la leche será pasada inmediata y directamente a la lechería. A ésta no deberán entrar los ordeñadores que traigan la leche.

En todo el transcurso desde el ordeño hasta su llegada a la lechería, el producto será protegido contra las causas de contaminación.

6. LECHERÍA Y PREPARACIÓN DE LA LECHE DE PRIMERA CALIDAD CERTIFICADA.

ART. 159. En todo establecimiento productor de leche de primera calidad certificada habrá una lechería, o sea un local a propósito, donde se manipule y prepare la leche para la venta. Ella consistirá por lo menos en dos piezas construidas totalmente de material (obra de fábrica), una destinada a la limpieza y esterilización de envases, recipientes, útiles, etc., y la otra a la mezcla, filtrado, enfriamiento, conservación y envase de la leche.

ART. 160. La lechería estará próxima al establo, pero no en comunicación con él.

En cuanto a su emplazamiento, orientación, ubicación respecto de otras instalaciones, locales o lugares y estado y mantenimiento del terreno circundante, habrá que llenar las condiciones indicadas para el establo, en lo que le sean aplicables.

Será amplia, bien ventilada, seca, fresca, con abundante luz natural, de fácil limpieza y desinfección y completamente construida de mampostería. Todo su interior estará recubierto de revestimiento de material (obra de fábrica), liso, impermeable, blanco y lavable. Los ángulos de las paredes entre sí y con el piso y cielo-raso serán redondeados. Satisfará, por lo demás, todas las condiciones establecidas en los artículos 63, 64 y 65, en cuanto le sean aplicables.

No se hallará en comunicación directa con habitaciones de personas.

Cada subdivisión de la misma estará provista del equipo y elementos necesarios para los fines a que se destina.

En ella no se introducirá ni manipulará otra leche más que la de primera calidad certificada, ni se introducirá ni tendrá nada que no sea necesario para tratar esta leche.

ART. 161. En seguida de venir la leche del establo, se mezclará, se filtrará nuevamente, se enfriará a diez grados o menos y se envasará en las botellas en que será entregada al consumidor, que serán inmediatamente cerradas y selladas en la forma en que debe recibirlas.

Desde entonces, la leche será mantenida continuamente a diez grados de temperatura o menos.

ART. 162. No se mezclará la leche de distintos ordeños, aunque éstos sean del mismo día, debiendo venderse aparte la de cada uno.

ART. 163. La leche envasada y lista para la venta será tratada en forma que los envases no se ensucien exteriormente. Las botellas o recipientes estarán perfectamente limpios al entregarlos al consumidor.

ART. 164. Todos los recipientes usados en el ordeño, recolección, filtración, mezcla, enfriamiento, medida y envase de la leche, así como los filtros, serán de chapa de hierro o acero sin costura y estañados en capa gruesa. Los refrigeradores, máquinas de envasar, etc., serán del mismo material en las partes que entren en contacto con la leche.

Recipientes y todos los útiles y maquinaria serán de fácil limpieza y desinfección y se hallarán siempre en buen estado de conservación. Se considerará que no lo están, cuando por sus condiciones la limpieza y desinfección no puedan hacerse fácilmente.

ART. 165. Los recipientes, utensilios y máquinas de que se trata en el precedente artículo serán mantenidos siempre en perfecto estado de limpieza.

En seguida de usarlos serán limpiados en la forma indicada en el artículo 26.

Los filtros, telas, paños, toallas, etc., usados en el ordeño y para el secado de útiles y recipientes que se hallen en contacto con la leche, después de bien lavados y sometidos a la ebullición, serán esterilizados a seco a 120° de temperatura por lo menos.

Después de lavados y limpios, los útiles y recipientes hasta de sesenta litros de capacidad que entran en contacto con la leche, serán esterilizados de igual manera.

Todos los útiles, máquinas y recipientes de mayor tamaño, después de limpiados en la forma ya indicada, serán esterilizados con agua hirviente o a chorro de vapor bajo presión y después secados con trapos esterilizados.

Todo lo mencionado en el presente artículo, después de esterilizado, será resguardado de contaminaciones hasta el momento de usarlo nuevamente.

ART. 166. Durante el trabajo, las personas ocupadas en la lechería vestirán pantalones o sobre-pantalones, saco cerrado y largo o delantal y gorro, todo blanco, lavable y limpio. Cada persona deberá estar provista por lo menos de tres mudas de esa ropa.

Mientras estén ocupadas, esas personas tendrán sus manos y antebrazos descubiertos y perfectamente limpios.

7. ASEO Y ESTADO SANITARIO DE LAS PERSONAS QUE INTERVIENEN EN LA PRODUCCIÓN DE LECHE DE PRIMERA CALIDAD CERTIFICADA.

ART. 167. Esas personas serán aseadas y observarán en todo la mayor limpieza posible.

La administración sanitaria podrá exigir que las que no satisfagan estas condiciones sean excluidas del establecimiento.

ART. 168. Estarán libres de enfermedades contagiosas que puedan transmitirse por la leche y de las que se mencionan en el artículo 99.

Antes de entrar a formar parte del personal del establecimiento, tendrán que proveerse de un certificado de revisación médica expedido por la administración sanitaria. Ese certificado se renovará cada seis meses.

La inobservancia de estas disposiciones será penada con multa de cien pesos, sin perjuicio de prohibirse la introducción y venta de la leche en la ciudad mientras ella no sea cumplida.

ART. 169. No estarán en contacto con otras personas afectadas de enfermedades contagiosas de las indicadas en el artículo precedente.

Los que lo hayan estado no deberán intervenir en las faenas que les correspondan, hasta después de ser autorizadas por la administración sanitaria.

La infracción de este artículo dará lugar a las medidas indicadas en el artículo precedente.

ART. 170. El propietario está obligado a avisar a la administración sanitaria de todo caso de enfermedad que se produzca en su establecimiento o entre las personas del mismo, acompañando un certificado médico en que conste la enfermedad de que se trata, si el enfermo no puede presentarse a ella para ser examinado.

La inobservancia de esta disposición será penada con multa de doscientos pesos, si la enfermedad no es contagiosa, y con la prohibición definitiva de introducir y vender la leche en la Capital, en caso de tratarse de alguna de las enfermedades contagiosas indicadas en el artículo 168.

8. VIGILANCIA SANITARIA DE LOS ESTABLECIMIENTOS PRODUCTORES DE LECHE DE PRIMERA CALIDAD CERTIFICADA Y ESTÍMULOS PARA LOS MISMOS.

ART. 171. Un veterinario inspector inspeccionará dichos establecimientos por lo menos una vez por mes.

La administración sanitaria podrá disponer que tales inspecciones se repitan cuantas veces lo estime conveniente o necesario.

El veterinario, además de los animales, inspeccionará el campo, los edificios e instalaciones, los forrajes, las aguas, las máquinas, envases y, en general, todo lo que haya que tener en cuenta en la producción de leche higiénica, y vigilará asimismo el aseo y estado sanitario de las personas y los procedimientos usados en esa producción.

Podrá recoger muestras de aguas, leche, forrajes, etc., cuantes veces lo estime necesario o conveniente.

Los gastos de viaje, hospedaje y comida del veterinario en las inspecciones serán costeados por los propietarios de los establecimientos. En caso de negativa a abonar estos gastos en la forma y plazos que fije la administración sanitaria, ésta podrá prohibir la introducción y venta de la leche en la Capital.

ART. 172. A los establecimientos que no llenen las condiciones prescritas en esta ordenanza en cuanto a instalaciones e implementos no se les permitirá introducir ni vender en la Capital leche de primera calidad certificada.

En cuanto a su estado y funcionamiento, el inspector clasificará por un sistema de puntos que fijará la administración sanitaria, y por separado, todos y cada uno de los elementos que deben tenerse en consideración al producir leche higiénica. Esa clasificación se hará en cada visita o inspección del establecimiento y de ella se entregará siempre una copia al interesado.

Se considerará en condiciones deficientes el establecimiento cuyos puntos parciales no sumen en total el 85 por ciento por lo menos del total máximo fijado por la administración sanitaria.

La clasificación de *deficiente* será seguida de un aviso al interesado, para que trate de salvar las imperfecciones existentes. Un mes después de la primera clasificación de

deficiente se procederá a una nueva inspección y clasificación, y, si el resultado de ésta es el mismo, no se permitirá la introducción y venta de la leche respectiva en el municipio.

A los establecimientos cuya clasificación total no pase del 75 por ciento se les prohibirá inmediatamente esa introducción y venta.

ART. 173. Los interesados podrán poner en las etiquetas de los envases, en los lugares de venta, en los avisos en que ofrezcan su producto, etc., las clasificaciones obtenidas por sus establecimientos, así como las proporciones de gordura y de microbios de la leche que venden. Pero siempre que lo hagan, serán las últimas clasificaciones obtenidas a esos respectos de la administración sanitaria las que deberán hacer constar.

La administración sanitaria podrá publicar las clasificaciones obtenidas por los establecimientos y sus productos, a fin de que el público sepa cuáles son los mejores.

Anualmente la administración sanitaria discernirá un premio, consistente en mil pesos m. n. y un diploma, al establecimiento que haya conseguido más altas clasificaciones en el año y cuya leche durante el mismo plazo haya sido de mejor calidad. Para esto se tomará en consideración las doce planillas de clasificación más alta de cada establecimiento y el resultado de los exámenes de por lo menos doce muestras de leche de cada uno, tomadas más o menos al mismo tiempo en todos ellos. No se tendrán en cuenta las planillas de clasificación correspondientes a inspecciones pedidas por los interesados ni los exámenes de leche solicitados por ellos. Se considerará leche de mejor calidad la que supere en mayor grado las condiciones establecidas en el artículo 2. Este premio no empezará a discernirse hasta después de pasado un año de existir por lo menos dos establecimientos productores de leche de primera calidad certificada.

ART. 174. Las condiciones enunciadas en este capítulo en cuanto a los establecimientos implementos y procedimientos de lechería son las mínimas que deben cumplirse. Pero los interesados podrán apartarse de ellas, siempre que sea para mejorarlas o superarlas del punto de vista higiénico, sin afectar los procedimientos de contralor sanitario, y previa aprobación de la administración sanitaria, quien decidirá sin apelación sobre el carácter de los cambios o innovaciones propuestos.

CAPÍTULO X. TAMBOS URBANOS.

ART. 175. Los tambos que se establezcan en la capital después del día de promulgación de la presente ordenanza estarán constituidos cuando menos, por el establo, el local de manipulaciones, un local de despacho que satisfaga las condiciones especificadas en el Capítulo VI, el depósito de forrajes y un "paddock" para el ejercicio de las vacas y estarán provistos de un depósito adecuado para el estiércol.

ART. 176. El establo será todo de mampostería y hierro. No podrá haber en él otras obras de madera más que las puertas y ventanas.

Estará provisto de cielo-raso de acero esmaltado o de mampostería, liso y de color claro. En sus partes más bajas, éste se hallará a una altura de 5 metros sobre el piso por lo menos.

En todo lo demás (construcción, disposición y naturaleza materiales del edificio y de sus instalaciones interiores, ventilación, humedad, temperatura, mantenimiento, limpieza, servicio de agua, etc.) habrá que satisfacer en cuanto a este establo las condiciones enunciadas en los artículos 122 a 137.

ART. 177. El local de manipulaciones o lechería podrá estar en comunicación con el puesto de venta por intermedio de una puerta que se abrirá sólo para pasar y provista de mecanismo de cierre automático, pero no deberá estarlo con el establo, ni con habitaciones, ni con el depósito de forrajes. En todo lo demás, la lechería responderá a las condiciones enunciadas en los artículos 159 a 166 y en los en ellos mencionados.

ART. 178. El depósito de forrajes será todo de mampostería, interior y exteriormente revocado y de acuerdo en todo lo demás con lo establecido en el artículo 119.

ART. 179. El "paddock" o corral de ejercicio de las vacas será al aire libre, tendrá por lo menos 10 metros de diámetro en cualquier sentido, estará provisto de piso blando y con drenaje y rodeado de cerco de superficie lisa y redondeada, todo de fácil limpieza.

Sus partes de madera estarán pintadas de blanco. El blanqueo se renovará toda vez que se halle en mal estado. Si es con cal, se repetirá por lo menos cada seis meses.

ART. 180. El depósito de estiércol será de mampostería, recubierto interior y exteriormente de espesa capa de cemento impermeable o de material análogo y tendrá tapa metálica, caño de ventilación y buen drenaje.

ART. 181. Todo el terreno libre de edificios que ocupe el tambo, exceptuado el "paddock," estará recubierto de piso sólido, impermeable, bien drenado y liso, esto último hasta donde lo permita la estabilidad de la marcha de los animales.

ART. 182. A distancia de quince metros del establo y de la lechería no habrá estercoleros, letrinas, depósitos de residuos, gallineros, caballerizas, etc., ni nada que dé malos olores o atraiga moscas en abundancia.

ART. 183. Las vacas permanecerán sueltas en el "paddock" de ejercicio por lo menos tres horas diarias, salvo que el mal tiempo no lo permita.

ART. 184. En cuanto al estado sanitario de las vacas, su alimentación y ordeño, aseo y estado sanitario de las personas, mantenimiento y limpieza del establecimiento y de los animales, manipulaciones de la leche y, en general, en cuanto a todo aquello para lo cual no se hayan fijado condiciones especiales en este capítulo, los tambos urbanos llenarán todas las establecidas al respecto para los establecimientos productores de leche de primera calidad certificada, en lo que le sean aplicables.

ART. 185. Los tambos que se abran al público después de la promulgación de la presente ordenanza se considerarán como de primera categoría y deberán llevar en el frente el siguiente letrero, en grandes caracteres de molde: "Tambo de primera categoría."

Sólo esos tambos podrán llevar este letrero.

Después de dos meses de abierto el primero de esos tambos, todos los otros, establecidos antes de la promulgación de esta ordenanza, deberán llevar en su frente, en el lugar más visible y en grandes caracteres de molde, el siguiente letrero: "Tambo de segunda categoría."

ART. 186. Todo tambo de los existentes antes de la promulgación de la presente ordenanza, que después se reconstruya, amplíe o cambie de dueño, será considerado como establecimiento nuevo, y regirán para él las prescripciones de este capítulo, relativas a los que se establezcan después de dicha promulgación.

ART. 187. Los tambos modelos municipales arreglarán los precios de sus productos en forma que no puedan competir con los de los tambos de primera categoría.

CAPÍTULO XI. VIGILANCIA DEL COMERCIO DE LECHE.

ART. 188. La aplicación de esta ordenanza y, en general, todo lo relativo a la vigilancia sanitaria del comercio de leche y de sus derivados, estará a cargo de la Oficina Contralor de la Leche de la Administración Sanitaria.

ART. 189. Los productores o tamberos que envían leche de primera calidad a la capital permitirán que los empleados de la susodicha oficina recojan muestras de leche en el mismo tambo rural, en las estaciones ferroviarias de embarque o en cualquier otra parte, fuera y dentro del municipio, así como de las aguas usadas en sus establecimientos, y prestarán a esos empleados toda su cooperación, a fin de que la recolección pueda hacerse en la forma y con las garantías necesarias para descartar cualquier error o fraude y sin molestias personales injustificadas. La falta de cooperación en este sentido será considerada como una negativa a permitir la recolección de las muestras.

Iguales obligaciones tienen las empresas, establecimientos o personas que envíen leche de primera calidad a la capital, procedente de distintos tambos o establecimientos productores, corriendo por cuenta de ellos el asegurarse de que estos últimos

cumplan la obligación de permitir la recolección de las muestras en sus tambos o en el trayecto de éstos a la factoría o lugar de recibo de la leche por dichas empresas.

Los inspectores municipales podrán presentarse sin previo aviso a tomar las muestras, de modo que los interesados deberán disponer lo necesario a fin de que aún en su ausencia ellos puedan cumplir su misión.

ART. 190. Los gastos de ferrocarril, coche, hospedaje y comida que tengan que hacer los empleados encargados de recoger las muestras indicadas en el artículo precedente serán abonados por los tamberos o productores, si éstos envían directamente o por su cuenta la leche a la capital, o por las otras empresas o personas mencionadas en el mismo artículo, en caso de ser éstas las que remitan la leche.

En ningún caso, los tamberos o productores tendrán que abonar por tales conceptos más de 250 pesos anuales, si sus establecimientos se hallan a 100 kilómetros o menos de la capital, o más de 350 pesos, si éstos se hallan a más de 100 kilómetros de la capital, ni las empresas o las personas que envíen leche de varios productores tendrán que abonar anualmente más de esas sumas multiplicadas por el número de productores de quienes recojan la leche. El exceso será costeado por la municipalidad.

Esos gastos serán abonados después de cada intervención o viaje de los empleados municipales, en la forma y plazos que fije la administración sanitaria.

La administración sanitaria dispondrá que se recojan muestras de leche fuera del municipio sólo cuando sea estrictamente necesario para efectuar análisis comparativos con muestras de las mismas leches tomadas antes o después en la capital y tratará de que los gastos que deban costear los productores o remitentes se reduzcan al mínimum posible. Las muestras de agua se tomarán con ocasión de la recolección de las de leche.

Las infracciones de este artículo o del precedente serán seguidas de la prohibición de introducir leche a la capital, so pena de decomisarla a su arribo, a menos que los interesados abonen una multa de 100 a 500 pesos, según la gravedad del caso. A la tercera infracción del artículo 189, se prohibirá definitivamente la introducción y venta en el municipio de leche de primera calidad procedente del establecimiento respectivo.

ART. 191. Los propietarios de lecherías o sus representantes permitirán en cualquier momento la inspección de sus establecimientos por los empleados de la administración sanitaria, que podrán inspeccionar todos los compartimientos o secciones del establecimiento y todo lo que se halle dentro de los mismos, así como revisar los certificados médicos del propietario y de todo el personal, y a quienes deberán prestar la cooperación necesaria para que puedan desempeñarse en la forma que más convenga para evitar errores o fraudes y sin sufrir molestias personales injustificadas. La falta de cooperación en este sentido se considerará como una negativa a permitir la inspección.

Las mismas obligaciones, tiene toda persona que se dedique al comercio de lechería o que venda leche, en cuanto al local de que se trata en el capítulo V, las empresas o firmas que se dediquen a la pasteurización o higienización de la leche o a cualquier otra operación con ella o sus derivados, en cuanto a sus respectivos establecimientos, y los lecheros ambulantes, en lo que se refiere a sus vehículos en circulación o en depósito.

ART. 192. Toda persona, empresa, sociedad o firma que intervenga en cualquier forma en el comercio de leche dentro de la Capital, así como sus empleados, permitirán que en cualquier momento y en cualquier parte los empleados de la administración sanitaria examinen la leche que reciban, tengan o lleven y tomen muestras de la misma y de tantos recipientes como lo consideren conveniente, sin exigir retribución alguna, y les prestarán la cooperación indicada en el artículo 189, cuya falta será considerada como una negativa.

Las infracciones de este artículo y las del precedente tendrán las mismas penas que las del artículo 8. El establecimiento será clausurado en cada caso o no se per-

mitirá la circulación del vehículo, si se trata de éste, hasta que el interesado deponga su oposición o resistencia.

ART. 193. La administración sanitaria podrá establecer servicios de vigilancia permanentes en las usinas, fábricas, etc., cuyos productos de lechería se introduzcan o vendan en el municipio para consumo.

Ese servicio será costeado por las empresas cuando sus usinas o fábricas se hallen fuera del municipio. En este caso las empreaas estarán también obligadas a dar alojamiento conveniente a los empleados de la administración sanitaria.

Cuando ésta lo juzgue conveniente, según la importancia de los establecimientos mencionados en este artículo, podrá exigir que se habilite en ellos un local para laboratorio, provisto de los elementos necesarios para el análisis químico y bacteriológico de la leche y sus derivados.

ART. 194. Las muestras de leche de que se trata en los artículos 189 y 192 serán dobles y se lacrarán y sellarán en presencia de los interesados o sus representantes.

Cada una llevará una etiqueta con todos los datos necesarios para individualizarlas.

Si el interesado lo pide, se le entregará una tercera muestra igual a las dos primeras, envasada y preparada en iguales condiciones.

En seguida se levantará un acta por duplicado, en que consten todas las circunstancias y detalles necesarios para precisar el acto, y que será firmada por el inspector y el interesado. En caso de negarse a firmar éste último, se dejará constancia de ello en el acta y se hará firmar ésta por un testigo. Una de las actas se entregará al interesado.

Una de las dos primeras muestras será analizada lo más rápidamente posible en la oficina contralor de la leche y la otra será convenientemente conservada, para el caso en que el interesado promueva un peritaje contradictorio.

CAPÍTULO XII. PERMISOS.

ART. 195. Nadie podrá vender leche en la capital sin previo permiso de la administración sanitaria, bajo pena de cien pesos de multa, clausura inmediata del establecimiento respectivo, detención de los carros de reparto que se hallen en circulación y comiso de la leche consignada al responsable, o que éste tenga o intente vender.

Las personas que se propongan vender leche en la capital deberán presentar una solicitud de permiso a la administración sanitaria, en un formulario especial que ésta les proveerá, en que consten su nombre y apellido, su edad, nacionalidad y domicilio, la ubicación de su establecimiento, el número de litros de leche que venden diariamente, la calidad de la misma según las disposiciones de esta ordenanza, su procedencia y las horas en que la recibe, y el nombre, apellido, nacionalidad y edad de cada una de las personas que tenga empleadas en su negocio, y en que se comprometa a respetar y a cumplir las prescripciones de la presente ordenanza en las partes que le atañen. Además, el interesado acompañará a su solicitud su cédula de identidad, expedida por la policía de la capital, y con un retrato, un retrato suyo de perfil, suelto y de 5 por 5 centímetros y los certificados médicos de la administración sanitaria para él y cada uno de sus empleados.

El retrato suelto quedará archivado en la administración sanitaria, juntamente con los datos realtivos al causante.

La persona que adquiere un negocio cualquiera de lechería está obligada a cumplir todas las disposiciones de este artículo, aun cuando el que se lo venda ya las haya cumplido.

Desde que entre a regir la presente ordenanza, toda persona dedicada al comercio de lechería en el municipio estará provista del permiso aquí indicado.

ART. 196. Todo cambio de domicilio o de ubicación de los establecimientos será comunicado anticipadamente a la Administración Sanitaria.

Los cambios del personal empleado en el negocio se comunicarán inmediatamente a la misma, dando los nombres y apellidos de los empleados salientes y de los que entren a reemplazarlos y acompañando los certificados médicos de estos últimos.

Todas estas comunicaciones se harán por escrito.

ART. 197. No podrá habilitarse o usarse ningún carro de reparto de leche dentro de la capital que no se halle aprobado y registrado en la administración sanitaria, a cuyo efecto los interesados presentarán con anticipación a la misma la solicitud correspondiente.

No se aprobarán ni registrarán los carros mientras las personas o empresas por cuenta de quienes se hará el reparto no estén provistas del permiso establecido en el artículo 195.

Si la administración sanitaria lo estima conveniente, podrá exigir que los carros lleven fija en un lugar visible, en vez del número de registro pintado o a la vez que éste, una chapa con dicho número, que ella entregará a los interesados mediante el pago de su costo y que tendrá el valor de un certificado de registro.

ART. 198. Dentro del municipio, nadie podrá ser repartidor ambulante de leche, por cuenta propia o por la de otros, sin previo permiso de la administración sanitaria, bajo pena de 100 pesos de multa, comiso de la leche y detención del carro por cuenta y riesgo del interesado (art. 91) hasta que la multa sea abonada y aquél se provea del permiso correspondiente.

A tal efecto, toda persona que se proponga repartir leche a domicilio presentará anticipadamente una solicitud de permiso a la administración sanitaria, en el formulario que ésta le proveerá, en que constarán todos los datos que debe llevar la libreta de que se trata en el artículo 97 y en que ella se comprometerá a respetar y a cumplir las prescripciones de la presente ordenanza en las partes que le atañen. Además, acompañará a su solicitud una cédula de identidad como la indicada en el artículo 195, dos retratos sueltos como los allí también indicados, uno para ser pegado en dicha libreta y otro para quedar archivado en la administración sanitaria, y un certificado médico extendido por la oficina respectiva de esta última.

La administración sanitaria extenderá el permiso en la libreta mencionada.

En cuanto entre a regir esta ordenanza, todos los lecheros o repartidores ambulantes, deberán estar provistos del permiso aquí establecido.

ART. 199. Todo productor o lechero que se proponga introducir o remitir leche al municipio debe solicitar anticipadamente permiso a la administración sanitaria, en un formulario especial que ésta le proveerá. En su solicitud dará su nombre y apellido o la firma comercial del negocio, su edad, nacionalidad, domicilio, ubicación del tambo, término medio de vacas que ordeñe diariamente, raza de las mismas, término medio de producción de leche por cabeza, horas a que ordeñe las vacas, superficie de campo en hectáreas que ocupa con su tambo, superficie alfalfada o con otros forrajes artificiales, superficie de campo con pastos naturales, dirá si el campo es de su propiedad o lo tiene en arriendo, dando en este último caso el nombre del propietario, declarará el nombre de la estación ferroviaria de embarque de la leche, las horas en que embarca en ellas el producto de cada ordeño, el nombre de la estación más próxima a su tambo o por donde sea más fácil el acceso de personas a su establecimiento. Al mismo tiempo se comprometerá a respetar y a cumplir en las partes que le atañen las disposiciones de la presente ordenanza. A su solicitud acompañará una cédula de identidad, con retrato, expedida por la policía del lugar donde tenga su tambo, en que deberá constar su profesión, y un retrato suelto de perfil y de 5 por 5 centímetros por lo menos. Este retrato quedará archivado en la administración sanitaria. El permiso que se expida al tambero llevará el número de su registro en la administración sanitaria.

Si la leche que se ha de remitir a la capital es de primera calidad, también habrá que acompañar a la solicitud una o varias muestras de las aguas usadas en el establecimiento, recogidas y transportadas en la forma que indique la administración sanitaria, y una descripción del establecimiento y de los procedimientos aplicados en el mismo.

Si se trata de leche de primera calidad certificada, además de todo lo indicado en los dos párrafos precedentes y de los que deba exigir la administración sanitaria de

acuerdo con lo establecido en el Capítulo IX, deberá acompañarse un plano del establecimiento y de sus edificios e instalaciones.

Los permisos de los establecimientos que remitan leche de primera calidad certificada o leche de primera calidad serán renovados anualmente.

En cuanto entre a regir esta ordenanza, todos los remitentes de leche a la capital deberán estar provistos del permiso aquí establecido.

ART. 200. Las fábricas, usinas, etc., de lechería no podrán funcionar dentro del municipio ni vender sus productos sin previo permiso de la administración sanitaria, que solicitarán anticipadamente de la misma, dando los siguientes datos: nombre de la firma o empresa, ubicación del establecimiento, capacidad productiva del mismo y cantidad de leche con que empezará a funcionar, clase de productos que ha de preparar o con que ha de operar u operaciones a que ha de someter la leche y forma en que ha de vender sus productos (si por intermediarios o directamente al consumidor, etc.) y acompañando una descripción del establecimiento y de las maquinarias y sistemas aplicados, ilustrada con planos.

Las que se hallen fuera de la capital tampoco podrán introducir sus productos sin ese permiso previo. Estas deberán presentar para conseguirlo una solicitud igual a las otras, pero que contendrá además los siguientes datos: distancia del establecimiento a la estación de embarque de los productos, número de tamberos o productores de quienes recibirá la leche, efectivo total de vacas productoras de la misma y forma en que ha de transportar sus productos a la capital.

Unas y otras, en su solicitud de permiso se comprometerán a respetar y a cumplir las disposiciones de la presente ordenanza en las partes que les atañen.

Al entrar en vigencia esta ordenanza, las fábricas instaladas dentro o fuera del municipio, que introduzcan o vendan sus productos en el mismo, deberán estar provistas de nuevos permisos, de acuerdo con lo establecido en este artículo.

ART. 201. Para introducir o vender en el municipio, para el consumo, leches que hayan sufrido preparaciones o transformaciones especiales, tales como leches esterilizadas, maternizadas, kefir, koumis, yogurt, etc., deberá tenerse previamente un permiso especial de la administración sanitaria.

ART. 202. Desde la promulgación de la presente ordenanza, antes de abrirse un tambo nuevo en la capital, o de proseguir funcionando, después de reconstruído, ampliado o haber cambiado de dueño, alguno de los existentes, deberá solicitarse permiso de la administración sanitaria, en un formulario especial y con los requisitos indicados en el artículo 195 y para los establecimientos productores de leche de primera calidad certificada, en cuanto sean aplicables al caso.

ART. 203. La administración sanitaria podrá exigir además a toda persona, firma, empresa o compañía cuyos productos de lechería se introduzcan o vendan para el consumo en el municipio, o que intervenga en cualquier forma en el comercio de leche y sus derivados destinados al consumo en el mismo, cuantos datos o requisitos sean necesarios para asegurar el cumplimiento de esta ordenanza, comprendida la presentación de títulos de propiedad, contratos de sociedad o arrendamiento, recibos de alquiler, etc.

ART. 204. La administración sanitaria podrá prohibir temporariamente la introducción de leche al municipio procedente de establecimientos o regiones donde exista alguna epidemia o epizootia que constituya una amenaza para la salud de los consumidores del producto.

ART. 205. La Administración sanitaria podrá señalar o fijar los lugares por donde deberán ser introducidos la leche y sus derivados destinados al consumo en la capital.

ART. 206, inciso 1. No se otorgará ningún permiso sin cerciorarse primero de si el solicitante tiene en las condiciones establecidas en esta ordenanza todos los elementos necesarios para el comercio o trabajo a que se va a dedicar.

Inciso 2. La leche que llegue al municipio de establecimientos o remitentes sin permiso o a los cuales se les haya retirado éste temporaria o definitivamente, caerá en comiso, en cualquier parte donde se encuentre.

Inciso 3. La repetición de las infracciones o faltas se considerará siempre como circunstancia agravante.

Inciso 4. A los que se nieguen abiertamente a dar cumplimiento a cualquiera de las disposiciones de la presente ordenanza, se les retirarán los permisos correspondientes y se les clausurarán los establecimientos, si se hallan dentro del municipio.

CAPÍTULO XIII. INSTRUCCIONES, CONSULTAS Y ANÁLISIS GRATUITOS.

ART. 207. La administración sanitaria preparará, hará imprimir y distribuirá gratuitamente a los interesados instrucciones sobre la manera de producir leche higiénica y de tratarla hasta el momento de ser consumida, atenderá en la misma forma cualquier consulta que se le formule respecto de esas cuestiones y asesorará sobre el terreno a quienes lo soliciten y abonen todos los gastos del técnico que a ese efecto se comisione.

Analizará también gratuitamente toda muestra de leche que se le envíe, así como de las aguas empleadas en la alimentación de los animales de lechería o en la limpieza de recipientes y utensilios usados en la misma industria, siempre que ellas sean tomadas y remitidas en las condiciones que ella indique, a cuyo efecto los interesados deberán dirigirse primero a ella, por escrito o verbalmente, pidiendo instrucciones.

Todos estos servicios serán prestados a las personas del gremio de lechería que tengan sus establecimientos en la capital, a las que los tengan fuera de la misma y dentro del radio de aprovisionamiento de la ciudad y, en general, a todas aquellas que puedan contarse entre sus posibles proveedores.

ART. 208. A las personas que por cualquier motivo no puedan hacerlo por sí mismas y que lo soliciten, se les redactarán en la Oficina de Contralor de la leche los documentos escritos que deban presentar al dirigirse a ella en cualquier sentido.

CAPÍTULO XIV. DISPOSICIONES TRANSITORIAS.

ART. 209. Las partes de esta ordenanza relativas a la leche de primera calidad certificada, a la leche de primera calidad y a los tambos urbanos entrarán a regir desde la fecha de su promulgación. Todo lo demás, a los dos años de la fecha de su promulgación.

ART. 210. El D. E. reglamentará la presente ordenanza.

ART. 211. Deróganse todas las disposiciones que se opongan a la misma.

The CHAIRMAN. These papers really constitute what might be called a symposium, and may be discussed as such at this time. I will therefore ask if any one here desires to make any remarks in regard to the papers that have been read.

Dr. SEDGWICK. Mr. Chairman, there are one or two small points in the way of addition that it seems to me might be made. In the first place, it has not been pointed out that by changing values we can add materially to some of our food supplies. It has lately been noted in the newspapers that in New York horseflesh is being recommended, or at least allowed for sale—a very proper procedure, as it seems to me, and I personally look forward to the time when a good many animals not now eaten will be regarded as good food.

Another point, it seems to me, is very illuminating, and that is in confirmation of Dr. Laspiur's statement that transportation has done so much for us that it may be said to have conquered famines. I had occasion some years ago to write for a youths' journal a paper on the conquest of famine, and I was very much struck with the

fact that since we have good transportation the important civilized and accessible portions of the world have had no famine. Of course, we all remember the terrible famines in Ireland in 1846–7, or 1848, or thereabouts, and as far as I know that period was the last period of terrible famine along the Atlantic or Pacific coasts, barring, perhaps, certain places in China and Japan. I suppose that if in 1847 they had had the means of transportation which we have to-day—certainly if they had had the means of cold storage, canning, and all that has come up since our Civil War—the awful mortality of Ireland would never have happened. So that this procedure of canning and cold storage and other methods of food preservation, added to transportation, have, for the time being at any rate, brought about a condition which we may well call the conquest of famine. On the other hand, that man would be foolish who did not give heed to the predictions of Sir William Crook or to those of Malthus, and keep his eye well to windward, watching for improvements and betterments of the food supply. Famines still occur, but they do not happen when a charitable public is able to send food. It was not able to send food in 1847 to Ireland; it would be able to send it to-day and send it in great abundance. Those are very small points, but the paper is so interesting I could not refrain from adding them.

The CHAIRMAN. Does any one wish to speak on this very interesting subject? If not, the other paper on the program will be read by title, as the writer is not present.

VULGARIZACIÓN CIENTÍFICA—HIGIENE BUCAL.

Por JULIO L. CATONI.
Buenos Aires, Argentina.

Contribución al difundimiento de conocimientos útiles. Aunque es difícil comparar entre sí la distinta importancia de los diferentes órganos del cuerpo, puesto que cada uno de ellos es necesario a la economía y su falta produce una perturbación en su actividad regular, sin embargo bien puede decirse que la boca es el órgano más útil del cuerpo, pues a ella están encomendadas muy nobles funciones. En ella se encuentran los dientes que tienen, a su vez, importancia grande, pues significan casi todo para la digestión y constituyen una parte muy esencial de la cara como estética. Bien se sabe qué encantos pueden dar a una fisonomía que sea hasta repulsiva, una hermosa dentadura, como se observa también el caso contrario. Sin entrar a enumerar los varios órganos que entran en la formación de la boca daré un ligero repaso sobre los fenómenos objetos de esta cavidad. La masticación, la insalivación y la gustación se efectúan integralmente en la boca y son la primera faz de la digestión con la cual están en relación directa. La masticación produce la trituración de los alimentos que son de este modo mezclados más fácilmente a la saliva y a los otros jugos digestivos. Las primeras modificaciones que sufren los alimentos en su constitución química y que tienen por consecuencia rendir los asimilables

son debidos a la acción de la saliva, líquido segregado por las glándulas diferentes que existen en la boca. En la tonación desempeña también un papel importante aunque el verdadero productor de la voz es la laringe; la faringe y la boca constituyen un tubo adicional que no toma parte en la emisión de los sonidos que vienen directamente de la laringe, pero sirve a darles articulación. Los fenómenos de masticación que acabo de mencionar y que se efectúan con la boca y los dientes son la primera faz de la digestión. Ahora bien, ya conocidos a grandes rasgos el objeto y fin de la boca debemos suponer que estando en buenas condiciones debe llenar su cometido en forma ventajosa para el organismo, siendo por lo tanto útil y aprovechable para el estómago e intestino el bolo alimenticio recibido, los cuales podrán asimilar con facilidad el alimento bien preparado aprovechándolo en su casi totalidad.

En el cumplimiento de estas operaciones entra el valioso concurso de los dientes, factor importante; justo es pues que me dedique a ellos, verdadero objeto de mi artículo y que demuestre la gran importancia de su buena conservación por medio de las reglas higiénicas tan sencillas, las cuales a su vez redundan en beneficio directo de la cavidad bucal a la cual pertenecen. El niño nace sin dientes; cuando su naturaleza adquiere alguna consistencia, que es a los 7 meses más o menos, comienza a efectuarse en él, la erupción de los primeros dientes, los cuales en los sucesivos, continúan haciendo su aparición hasta los dos años, y algunas veces hasta después de la época en que el niño ya es apto para alimentarse por sus propios medios; la primera dentadura del niño que es temporaria, consta de veinte dientes y muelitas, número suficiente para llenar el espacio reducido de la boca infantil. Con esa dentadura provisoria el niño tiene que hacer frente en la edad de los continuos cambios, a la gran tarea de la alimentación, pues en esa edad todos los órganos se desarrollan y exigen del cuerpo gran reserva de elementos constitutivos, esos dientes desempeñan también un gran papel, el de la formación de los dientes permanentes. Es evidente que como fenómeno fisiológico la dentición participa de ese orden y concierto con que la naturaleza reviste todas sus manifestaciones y que el nuevo ser no tiene necesidad de masticar, no se completa su aparato dentario. Hasta tanto el desarrollo lo exija, no desgastará el diente permanente al temporario para expulsarlo y sustituirlo. El nuevo germen no solo tiene por objeto el triturar los alimentos como parecería a primera vista, sino que tiene también el de guardar el sitio a su sucesor; el diente sustituto que en el fondo del maxilar se desarrolla socava a su predecesor por las raíces, las cuales cabalgando y aprisionando la corona del nuevo germen le marcan la senda que invariablemente debe recorrer, al fin de cuyo ciclo el diente de leche ha perdido por completo su raíz por cuyo motivo se engendra en el público la falsa idea de que los dientes de los niños no tienen raíz. Cualquier anomalía de la dentición temporal se trasmitirá de una manera más o menos pronunciada a los dientes definitivos o viceversa, una primera dentición normal es seguida de otra normal también, pues muy raras veces esa tiene por consecuencia anomalías de la dentadura definitiva. Esta regla fisiológica con que se realiza la evolución dentaria, tiene numerosas excepciones, unas debidas a enfermedades intra o extrauterinas, y la mayor parte de las veces, a la extracción prematura de los dientes de leche.

En estos casos la mala posición dentaria es la consecuencia más frecuente y lamentable, puesto que el que extrae la muela extemporáneamente es el ocasionador de un verdadero desorden en la boca. Al extraer un diente temporal, antes de su caída, se deja amplitud al sucesor para que tome cualquier dirección, puesto que se le quitan las guías seguras que le hubieran conducido por camino recto a su justo lugar. Quiere decir que es a todo trance indispensable la conservación de los dientes de leche en el niño, puesto que su extracción no sólo perjudica a su masticación, sino a los dientes permanentes en su posición, evitando así a veces su erupción, por destruirse o arrastrar el germen con ella.

Después de los seis años hacen su aparición las primeras grandes muelas llamadas por este motivo los molares de seis años, efectuándose casi simultáneamente el cambio

de los dientes incisivos, es ésta una edad crítica, pues la infancia entra en la edad escolar, edad que a la vez es época de los grandes desgastes orgánicos exigidos tanto por el desarrollo como por las fatigas de las tareas escolares, que aunque proporcionadas a la edad, no dejan de hacerse sentir en el organismo infantil. En este período la infancia necesita del concurso de todos sus órganos nutritivos para hacer frente a los procesos de transformación, como así a sus múltiples enemigos. Hasta los 12 años continúan los cambios dentarios, época en que puede decirse es ya definitiva y estable la situación de los dientes, salvo pequeñas modificaciones complementarias de crecimiento como del maxilar, que hasta la salida del tercer molar o del juicio sufre alguna pequeña modificación. Este molar hace erupción entre los 18 y 25 años salvo raras veces que sale antes a causa de haber sufrido la boca extracciones tempranas del primer o segundo molar.

Ahora ya conocidos someramente los procesos de la anatomía dentaria, debo explicar que no es suficiente tener dientes en la boca para poder masticar, sino que a esos dientes, cuyo valor es inestimable, se les debe cuidar con esmero para que la utilidad que presten sea máxima y no mínima, y para ello voy a describir todos los efectos posibles de producirse en una boca descuidada, pudiendo aceptarse desde luego que la mayoría de los descritos existen en alto porcentaje en el mundo.

Los hombres de ciencia, activos higienistas, nobles de corazón, anhelosos de difundir enseñanzas provechosas entre el pueblo con objeto de hacer obtener mayor facilidad en la vida y mayor aprovechamiento de las energías humanas, evitando con ello los entorpecimientos que ocasionan las enfermedades y propendiendo con ellos al mejoramiento de nuestro estado social, aconsejan sabiamente reglas sobre diferentes regímenes de vida y alimentación; pero qué provecho puede sacar de esas enseñanzas el que las lea, si antes que esas nociones debe poseer las elementales, o sea conocer los medios para poder llevar a cabo con buen éxito y en buenas condiciones aquéllas, comenzando por poseer una boca idealmente limpia y dientes íntegramente sanos? La base de la buena alimentación estriba sencillamente en eso.

La limpieza de la boca del ser humano debe practicarse desde sus primeros días, es una provechosa práctica de las madres limpiar las encías y lengüitas de sus hijos con una gasa limpia, hervida y humedecida en agua hervida también, con objeto de desembarazarle de las aglomeraciones saburrosas que se forman en los niños, especialmente después de las horas de reposo: esa práctica evita que el párvulo ingiera esas concreciones nocivas sirviéndole a la vez de tónico a la mucosa gingival, sobre todo cuando comienzan a brotar los primeros dientes, evitando así las inflamaciones y la mayor parte de los accidentes de la dentición, debidos, casi siempre, a falta de higiene. Cuántas madres no conocen las bocas de sus hijitos sino hasta que se les ha llamado la atención sobre la salida del primer diente, el cual siempre es recibido como un acontecimiento; al revés de otras madres que se desviven por verles dientes a sus hijos y, anhelosas de que eso suceda, consultan a amigas y vecinas qué medios son más eficaces para favorecer la salida de los dientes, no faltando comedidas que aconsejen pociones y jarabes de dudosa eficacia, casi siempre mal sanos y otras, menos temerarias aconsejan hacer chupar al nene dientes de los animales, collares de ámbar y colgar al cuello de la criatura amuletos de las especies más variadas? En el siglo de hoy deberían desaparecer esas ignorancias.

Desde que los dientes se van colocando en sus respectivos lugares son ya acreedores de la limpieza más minuciosa la cual se hará con el concurso de cepillos fabricados exprofeso para niños con objeto de desembarazar los intersticios de los dientes y la boca de los residuos alimenticios. Estas limpiezas deben hacerse con especialidad en la noche antes de acostarlos.

Suponiendo que los niños han de permanecer 8 o 10 horas durante el sueño con la boca en completo reposo e inmovilidad, encontrándose ésta llena de residuos de los alimentos ingeridos durante el día, tienen que producirse fermentaciones y descomposiciones altamente favorecidas por un ambiente húmedo y tibio. Estas altera-

ciones del contenido bucal son casi siempre de carácter ácido, quedando estacionadas en forma de papillas, en el cuello de los dientes, vestíbulo de la boca y superficie de la lengua acumulándose, noche tras noche, hasta formar verdaderos cálculos, enemigos de las encías a las cuales desalojan de los dientes imitándola en alto grado y dando lugar a la aparición de inflamaciones de diversa índole; favorecen la acidez constante de la saliva pudiendo esta acidez penetrar en la primera grieta del esmalte de los dientes dando origen a la formación de la carie o picadura del diente, la cual arrastra al mismo fin a sus compañeras, determinando en poco tiempo la pérdida o inutilidad casi total de esos órganos.

La boca, en ese estado, puede decirse que ya es albergue de una regular cantidad de microbios, los que están en acecho de cualquier oportunidad para hacer de las suyas; debido a las caries comienza la inflamación de las glándulas, que no es otra cosa que la infiltración séptica de microbios en esos órganos, originando esto un peligro muy grande, pues ellos se ven debilitados en su poder ofensivo contra los gérmenes nocivos, y quedan completamente imposibilitados, en su poder defensivo dejando en el mayor desamparo a las mucosas bucales y el organismo. Estas mismas glándulas, al inflamarse, pueden comprimir el conducto auditivo, impidiendo la entrada del aire a él, originando por consecuencia diversos trastornos en los oídos; pueden dar lugar también a la formación de vegetaciones adenoideas conocidas por la mayor parte del público ilustrado, tan peligrosas, pues impiden al niño respirar por la nariz, obligándolo a respirar indebidamente por la boca; la nariz no es sólo un adorno, tiene por objeto atender la respiración, filtrando los gérmenes nocivos y calentando el aire antes de que llegue a nuestros pulmones; en cambio la respiración bucal la priva de esos beneficios, esas mismas vegetaciones, sobre todo las nasales, debido a su expansión, modifican y comprimen los huesos de la nariz, estrechando de tal modo los canales que dan paso al aire que luego el calibre permanente de dichos huesos es insuficiente para dejar pasar el aire necesario, dando al niño un aspecto corporal raquítico e impidiendo su expansión torácica debida.

Estos son algunos de los peligros locales de la boca; ahora veamos los peligros de la mala nutrición. Ante todo, un niño con dientes cariados no puede masticar bien, pues sus dolores y la falta de integridad de aquéllos no se lo permiten; los alimentos que ingerirá, en esas condiciones, aparte de estar mal masticados irán mezclados con los residuos nauseabundos que contiene su boca, cuellos de sus dientes y encías infectando el alimento y neutralizando la acción de los jugos gástricos, ese niño tiene que tener forzosamente, una merma enorme debido a esa forma anormal de nutrirse y en lugar de abastecer a su organismo de elementos constitutivos, lo obliga a devorar los que tiene, creando una falta de equilibrio orgánico, originario de un estado anémico y raquítico, quedando ese organismo predispuesto en cualquier momento a sucumbir a la acción de los múltiples enemigos que lo acechan.

La falta de ese equilibrio lentamente acaba por poner triste al niño, privándose de esa alegría tan natural en la infancia; los dolores acaban por irritarle los nervios sensorios volviéndolo irritable y poco accesible, dándole la anemia, debida a la infección de su sangre un aspecto enfermizo; perdiendo el brillo de sus ojos y presentando un aspecto pálido tan desagradable y tan poco característico de la niñez, la cual siempre es y debe ser un exponente de robustez y lozanía.

Puede adquirirse en ese peligroso período cualquiera de las terribles enfermedades que azotan la infancia, como son la difteria, fiebre tifoidea, fiebres gástricas, etc., cuyo resultado lógico es el empeoramiento de las condiciones orgánicas, hallándose por consecuencia ese cuerpo más inhabilitado para luchar contra la devastación. Es entonces que la terrible tuberculosis tiene oportunidad espléndida para adueñarse de ese organismo, no se necesita para ello más que un leve resfrío, que degenerará en una congestión pulmonar, la que si no es atacada a tiempo se extiende ocasionando los verdaderos estragos de una pulmonía infecciosa muy grave de por sí, y que si llega a curar ¡pobres pulmones!, quedan casi siempre convertidos en el palacio más apto para vivienda y asilo seguro de los bacilos de Koch, los que formarán sus colonias

sin impedimentos de ningún género, devorando en poco tiempo ese pobre organismo ya casi inútil por todos los achaques y accidentes sufridos, exponiendo con tal hecho el inmerecido y triste final de una juventud que era toda una promesa para el futuro.

Muchos de los padres que lean estas líneas no habrán llegado a suponer que la responsabilidad moral que tienen sobre sus hijos se extienda hasta estos límites. Sin embargo es así.

En Europa civilizada existen y funcionan en todas las ciudades y pueblos cuerpos médicos escolares bien organizados, donde la boca es objeto de preferente atención y está encomendada al cuidado exclusivo de profesionales peritos, que no tienen otra misión que prodigar a los que necesitan esos cuidados especiales, se ocupan también de dar periódicamente conferencias a los niños sobre la gran importancia del cuidado higiénico de la boca y dientes, inculcándoles conocimientos y máximas suficientemente poderosos para que esos hombres de mañana se preocupen realmente de cuidar una cosa para ellos ignorada y de gran trascendencia en su vida.

Aquí y en regiones análogas, desgraciadamente, no han llegado todavía los beneficios de esas útiles instituciones y parte de esa enorme labor esta encomendada al médico, que en medio de su atareamiento diario, donde se ve obligado a ejercer todos los ramos de la medicina y cirugía, no le queda materialmente tiempo dedicarse a esa especialidad de la higiene y sólo lo hace en casos necesarios donde su presencia es exigida, limitándose casi siempre a enviar al paciente al dentista mejor especializado. Es entonces donde el dentista tiene oportunidad de hacer ver, por medio del caso práctico, al paciente o a sus padres, el estrago y las consecuencias de la falta de higiene. Momentáneamente éstos aparentan dar importancia a la cosa bajo el peso de las circunstancias, pero como esos consejos cayeron al azar en un momento accidental los olvidan con facilidad; en cambio, si ese niño hubiera tenido nociones y sus padres hubieran sabido que la higiene de la boca tiene importancia trascendental en el sostenimiento y conservación de la vida habrían dado más importancia al accidente sufrido y hubieran tratado de evitarlo en lo sucesivo. Entonces el único modo de conseguir algo en pro de estas enseñanzas es comenzar a dictar por medio de la prensa local tan empeñosa y decidida en la obra educativa, una cátedra de higiene haciendo conocer el objeto de determinados órganos, consecuencias distintas e inevitables de la falta de limpieza y cuidado de dichos órganos y medio para evitar su desperfecto y alteramiento propendiendo con ellos a su verdadera conservación.

En resumen definiré en pocas palabras todos los medios y cuidados necesarios para la buena conservación de los dientes, evitando con ello y por consecuencia el alteramiento de los demás órganos anexos.

Como he dicho, repito, desde la más tierna edad se debe vigilar la limpieza de la cavidad bucal, cuando los dientes ya han hecho su aparición y durante todo el transcurso de la vida. Esa limpieza debe efectuarse dos veces por día a la mañana al levantarse y a la noche antes de acostarse, a fin de que el ambiente de esa boca, sea lo más estéril posible; un cepillo de forma y dureza especial será el encargado de efectuarla con la ayuda de determinados agentes bajo forma de polvos de cualidades definidas, y que el más indicado a prescribirlas es el Dentista, después de previo examen de la boca del interesado. Si a pesar de esos cuidados se nota dolor o alguna pequeña, cariadura a veces imposible de evitar, se debe acuir sin pérdida de tiempo al Dentista a objeto de curarla y taparla, lo mismo si se nota que los dientes salen en mala posición o torcidos y las mandíbulas estan proyectadas hacia adentro o hacia afuera, se debe consultar igualmente al odontólogo.

La boca a pesar de esos cuidados, que no siempre serán efectuados con la debida energía y esmero, acumula sarro y depósitos llamados cálculos. Igualmente se debe acudir una vez por año a los buenos oficios del Dentista para que liberte a los dientes y encías de esos temibles enemigos.

En fin, para terminar, la boca debe ser objeto de la más constante atención en cualquier persona y durante todos los períodos de la vida, pues en todos esos períodos es igualmente útil; pero donde tiene mayor importancia la buena conservación de la

dentadura es en la infancia, vuelvo a repetirlo, sin cansarme, por ser ella la esperanza de un pueblo y por representar el futuro evolucionista de una raza y el perfeccionamiento de la generación que anhelamos todos.

La no observancia de la higiene buco-dentaria determina todas y muchas más alteraciones que las descritas, trayendo como consecuencia trastornos de efectos terribles. en la niñez, con su inevitable corolario de depresión mental. Es por lo tanto necesario hacer un llamado a los padres de familia sobre la activa vigilancia que deben ejercer en ese sentido sobre sus hijos, constituyendo, su indiferencia e impasibilidad al conocer todos esos peligros, la sanción social de un crimen de lesa humanidad.

Creo haber usado de medios suficientes, dentro de mi inutilidad literaria, y sin la facilidad y claridad que lo habría hecho un hombre de letras, para demostrar y hacer resaltar la imperiosa necesidad de aplicarse en la higiene bucal. Si algo consiguiera con ésto, tendría la satisfacción de haber sido útil, con mi modesto y pequeño aportamiento de nociones concernientes a mi profesión, a muchos que quizás hubiesen resultado perjudicados con su desconocimiento.

Through the courtesy of the writer there was presented to the congress at this session a copy of the following printed book:

Higiene dentaria del niño, por Carlos P. Berra, Dentista del "Cuerpo Médico Escolar." Cabaut y Cía, editores, Buenos Aires, 1916.

Adjourned at 4.30 o'clock.

JOINT SESSION OF SUBSECTION D OF SECTION VIII AND SUBSECTION 4 OF SECTION V.

NEW EBBITT HOTEL,
Tuesday morning, January 4, 1916.

Chairman, J. D. GATEWOOD.

The session was called to order at 9.15 o'clock by the chairman.
Papers presented:

Disposal of refuse. Papers by George A. Soper and William T. Sedgwick.

Collection and disposal of municipal refuse. Papers by J. T. Fetherston, Morris Knowles,[1] and J. W. Paxton[1].

The CHAIRMAN. The first paper, on a most interesting subject, "Disposal of refuse," is by Dr. George A. Soper, president of the Metropolitan Sewage Commission, New York City. Dr. Soper will please come forward and read his paper.

AVAILABLE METHODS FOR THE SANITARY DISPOSAL OF REFUSE.

By GEORGE A. SOPER,
Consulting Sanitary Engineer, New York.

The intended scope of this paper was indicated in the preliminary program of this meeting as follows:

VI. *Disposal of refuse.*—Under this topic there is a wide range of topics to be considered, viz, (1) sewage disposal, (2) garbage, (3) ashes, (4) night soil, (5) stable manure, (6) trade wastes, (7) miscellaneous refuse of the household, and (8) street cleanings. The collection, transportation and ultimate disposal of these classes of refuse will be considered, and incidentally the purity of rivers and other bodies of water.

When it is considered how small a topic may profitably engage one's attention, and how various and complicated are the chemical, physical, biological, sociological, political, economic, engineering, and administrative questions with which the present subject is involved, the magnitude of the undertaking which has been assigned to the author of this paper will become apparent. No attempt at thoroughness could be warranted within dimensions smaller than a series of volumes. Nor would such an effort be pertinent before the members of this congress had been given an opportunity to relate their experience and opinions. All that will be attempted is an outline of some of the main bearings of the subject as related, particularly to methods, the expectation being that the contributions of others will supply many details of present interest.

[1] Paper printed in vol. VI of the Proceedings of the Second Pan American Scientific Congress.

The term "refuse" is here used to cover broadly all liquid and solid waste substances produced in the houses and streets of cities, towns, and villages under ordinary conditions of occupancy.

Refuse is divisible for consideration into two general classes: I. Solid refuse, and II. Sewage. This division leaves something to be desired on the score of precision, but it is impossible to be scientifically accurate in the use of terms in dealing with the disposal of refuse, for there is no universal agreement among sanitarians with respect to them.

Sewage, which is the material customarily carried from its points of origin in underground pipes and drains, usually by means of a flow of water, can be finally disposed of in definite and effective ways. The means which are available for the collection have reached a point of perfection which leaves little to be desired. The processes which are available for final disposition have received a great deal of study in the laboratory and on a practical scale with the result that a large amount of information exists concerning the principles which must be followed in order to insure successful results. Sewerage and sewage disposal, therefore, represent a rather high state of development considered either as a science or as an art.

The disposal of solid refuse, on the other hand, has not yet emerged from that primitive state of development in which the experimental generally exceeds the certain result. Centuries older than the subject of sewage disposal, the current methods of to-day are not very far advanced over the methods which were in force in the time of Moses. Considering the fact that the sanitary disposal of refuse has materially affected the comfort and welfare of human beings ever since men ceased to live an uncivilized and nomadic existence, it would appear that the methods now available for the removal and final disposal of all classes of solid refuse should be well worked out and thoroughly understood. The truth is, however, that modern civilization has but recently come to recognize the importance of the subject and been able to focus the scientific attention upon it which is necessary in order that well-developed methods may be evolved.

I. THE DISPOSAL OF SOLID REFUSE.

While the sewage of a city is removed from the houses and streets where it is produced without the average inhabitant seeing or knowing even the routes which it follows, the opposite is the fact with regard to the disposal of the solid wastes. The garbage, ashes, papers, stable manure, and other solids are stored on the premises until they become no longer tolerable, then placed with their receptacles in the highway, from which they are collected in a noisy, dusty, odorous manner, hauled in foul and leaky wagons, often for long distances, through the city, and finally dumped at places which are offensive in the extreme. This is not the best practice, but it is the usual one; there is hardly a city to be found which is not guilty of some or all of the offenses named. It is unpleasant to mention these conditions, but it is necessary to recognize them, if more correct and suitable procedures are to be devised.

There is need of improvement in the manner of collecting the solid wastes and of disposing of them. The first is largely a matter of administration, the second chiefly a question of plant. If the wastes can be gathered properly to suitable points for disposal, it will be within the range of scientific effort to dispose of them without danger or offense. If the collections can not be made suitably, it will be hopeless to attempt to cope with the problem.

Suitable collections mean, first, appropriate receptacles and a correct use of them by the householder. This is always a difficult thing to accomplish. It is natural to throw refuse away carelessly and think no more about it. This course has been made practicable so far as sewage is concerned, by the invention of the water carriage system, but there is nothing comparable with the sewerage system which can be used for the solid wastes. The ashes, papers, floor sweepings, old cloths, bottles, cans, boxes,

and kitchen garbage must be put into receptacles, and these must be taken out of the house and emptied from time to time. Proper receptacles and a proper use of them constitute the first essential for the householder.

The duty of the municipality begins soon after the wastes are produced. It extends into the houses. The municipality should insist upon the kind of receptacle to be provided and what kinds of materials may and may not be put into them. There should be regulations specifying where and when the receptacles should be placed to facilitate their removal and emptying.

In some well sanitated cities the solid wastes are collected together in mixed condition; in others the householder is required to keep the ashes separate from the kitchen swill and from the papers and other materials. The regulations in respect to this matter should depend upon the way in which the wastes are to be disposed of. It has not been found that any appreciable hardship is imposed upon householders by such requirements. Separations at the house were first required in New York by the late Col. Waring many years ago, and are still insisted on in that city with its 5,500,000 inhabitants. The householders can be made to do a great deal of work which will facilitate the disposal of the solid wastes if they are treated fairly, and it is desirable that this fact be made use of to the full. Experience shows that it is desirable and feasible to insist that the house receptacles shall be placed for collection in situations which are accessible to the men who are charged with the duty of emptying them, and they are to be placed there on those days and at those times when the collectors are able to make their rounds. Compliance in these directions will be the more effective if there is no question as to the authority demanding it, and confidence that the collectors will do their part. There must be real authority and the public must be treated fairly.

One of the secrets of success in all branches of municipal refuse disposal lies in the mutual help which can be given by the public and by the city officers. No cleaning department, however efficient it may be, can keep a city clean if it does not receive the intelligent help of the citizens. The health department, the police, and the cleaning force should work together with mutual confidence and understanding. In no branch of city work is cooperation so necessary as here.

Contract and day labor.—The collection and disposal of solid refuse are sometimes done by contract and sometimes by a force in the regular employ of the municipality. In many cases the collections are made by the city and the collected materials turned over to a private firm for final disposition. Carts and wagons, too, often of unsuitable form, are used in either event; their main faults are that they are too high, too heavy, and too open. There is a good field for the employment of American ingenuity in the perfection of carts and wagons for the collection of solid refuse.

Traction is usually effected by horses, and this seems to be the cheapest plan, except when the vehicle can be operated for unusually long periods of time, or is employed on long hauls, in which event motors are the more economical. The particular type of wagon or cart to employ depends a good deal upon the material to be carried and the topography of the district. Whatever their design, the vehicles should be large, low, covered, and tight.

Carts have been designed for household receptacles so as to carry off the refuse in the containers in which it was first put, empty receptacles being left in their stead. There is the objection to this practice that it is seldom feasible to thoroughly cleanse the containers, and no one wants to receive a receptacle which has previously been used in a house where sickness has occurred. Wagons are sometimes provided with covers and a mechanical device for emptying the receptacle without causing the dust and odors to escape. This appears to be a practicable scheme and has much to recommend it. But it is to be noted that such vehicles generally require the householder to employ a special form of receptacle. Perhaps some will regard this as an advantage, for it does away with the use of such unsuitable receptacles as boxes, bas-

kets, and worn out cooking utensils, which, in spite of considerable pressure, are to be found in use in nearly all cities, to some extent, at the present time. The standard receptacle for garbage and for mixed garbage and ashes, in American cities is a galvanized iron can with a tight-fitting cover.

Collections should be made at regular intervals, and the days of collection should be scrupulously kept. The frequency of collection for garbage, when kept separate from ashes, should be not less than twice or three times per week, according to the season of year and climate. A somewhat longer period is permissible when the ashes and garbage are mixed.

Final disposition.—The most common methods of final disposition for household refuse are dumping, burning, and hog feeding.

In spite of the fact that the feeding of hogs with the garbage of cities is widely practiced, it can not be said to be wholly satisfactory. The idea of turning useless swill into valuable pork has attractions for the economist, but it can not be accomplished on a large scale in a way that is satisfactory to the sanitarian, judging by the efforts which have been made so far. A few years ago it was undertaken by a Prussian city, and although the scheme was carried out with characteristic German thoroughness, the plan was eventually given up. It was impossible to keep the hogs healthy and their quarters clean. Hog feeding is less objectionable when practiced on a small scale.

Notwithstanding its bad reputation, the dumping of household refuse on land when properly carried on has a great deal to recommend it. All dumping is not bad dumping, by any means. It may be said to be good or bad according to the place where the material is dumped and what is done with the deposits. Left to itself, a refuse dump may be one of the most objectionable nuisances to be found in the vicinity of a city. Properly cared for it may not be objectionable at all. Garbage alone can not, of course, be suitably disposed of in this manner, but garbage and ashes in mixed condition may be dumped, or ashes alone, or garbage, ashes, and rubbish.

It is a mistake to suppose that land whose level has been raised by deposits of refuse is a menace to health or unsuitable for any use. There are few cities of considerable size parts of which have not been filled in and built upon without evil consequences. In some of our great cities very large tracts have been recovered in this way and parks have sometimes been made of the districts so reclaimed.

Dumps should be drained to start with and leveled and covered with earth as the work of dumping progresses. If the process of filling is carried on in accordance with correct engineering and sanitary principles, it will not be objectionable.

Garbage can be composted to advantage, a fact which is much less generally understood in America than in Europe. The compost heaps need not be especially offensive nor located where the material is likely to cause complaint; the resulting material is likely to be of considerable value as fertilizer. Unfermented garbage is of little service as a manure.

Reduction and burning.—One of the most approved processes for the conversion of garbage into a useful commodity is known as reduction. Essentially this method extracts the grease by means of heat or gasoline, leaving a by-product which can be used as a basis for manure. There are some large plants which dispose of garbage by reduction; in fact, this method seems less suited to small cities and towns than to large places. Usually the works are owned and operated by a corporation which takes the city's garbage and disposes of it for a term of years upon the payment of a sum of money by the municipality.

Burning, or, as it is sometimes called, incineration, is generally regarded as one of the best, if not the very best, and most frequently applicable processes for the final disposition of household wastes. It has the advantage, so far as sanitary considerations are concerned, that it utterly destroys whatever it deals with. Further, burning is capable of dealing with garbage, ashes, and rubbish, so that, unlike reduction, the entire problem of disposing of these three classes of refuse is solved at one stroke. Finally, the heat produced by the flames can be turned to profitable account in the

production of steam and electric power and light. The furnaces which are suitable for this work may be of a size to accommodate the wastes of almost any municipality. For good results they must be skillfully designed and operated. In Europe, particularly in England and Germany, there are excellent examples of refuse destructors, as they are properly termed.

Utilization finds an encouraging field in the disposal of rubbish, for here are contained the metals, bottles, pieces of cloth, and other materials which, when separated from the mass in which they are cast away and brought together in quantities, have a market value. It is feasible and often desirable for the authority which is charged with the duty of disposing of rubbish to have it overhauled with the object of recovering the salable ingredients. In this direction, as in some others, useful lessons may be learned from the practices of private scavengers.

Private scavenging.—In practically all cities of the United States there are men who make a living by taking away for disposal the wastes of butcher shops, restaurants, and the garbage and ashes of private dwellings. Where there is no central scavenging force operating at the expense of the city, and this applies to hundreds of small cities and villages in the United States, the employment of private scavengers affords the only means which the householders have for getting rid of their solid refuse. Sometimes the scavengers operate under licenses issued by the health authorities; sometimes such permission is not required.

The operations of private scavengers are various and seldom sanitary, except in large cities. Depending upon the value of the material which is taken away, the scavenger either receives a sum of money for his services or gives a small amount. The work of collection is often done badly, and the system has many disadvantages, but the commercial aspect of the subject is developed in some cases to a surprisingly high state of perfection. The garbage is usually fed to hogs; the ashes are dumped; the rubbish is overhauled; and the salable materials are carefully collected into piles and stored until enough of each class has accumulated to be marketed to advantage, when it is shipped away.

The tendency of the times is to insist upon more frequent collections of solid house refuse, a better disposition of it, and a more centralized control of the whole subject. The future seems likely to see improvements in the operations available for collection and disposal in small communities as well as in large ones. There is certain to be a better recognition of the need of devoting intelligent care to the whole subject, and in view of the remarkable amount of attention which is being given all other branches of sanitary work, it seems not too much to expect that the collection and disposal of the solid refuse of municipalities will emerge from the neglected state in which it exists and take its place among other well organized municipal enterprises.

Encouragement for expecting improvement is found in the popularity which has recently attended the periodical cleaning up of cities of all sizes in the United States. In these "clean ups," as they are called, special days are set aside for the thorough cleaning of houses, yards, shops, alleys, and streets. They are not intended to be substitutes for the routine cleaning which is desirable, but are supplementary to it. Prizes are given for the best individual work, and school children are enlisted to act as inspectors and, it must be confessed, as educators. The campaigns carried on in this way have been full of practical value, for if they have laid what to some would appear to be unwise emphasis upon an occasional cleaning instead of upon the continuous care which a city should have, they have aroused the interest of many persons who could not have been persuaded to follow the better course at once. A thorough cleaning once a year is better than no cleaning at all, and in some cases, probably in many, the good beginning has been followed by sustained and productive efforts.

Night soil.—The removal of night soil is generally carried on by a force quite independent of other refuse collecting agencies. Sometimes this work is done by a health

department, but usually by small contractors licensed by the city and operating under more or less careful regulation. The material is removed from the privies and cesspools either by shoveling or pumping. Sometimes the work is done by so-called odorless excavating apparatus, if the quantity and consistency permit of it. It is customary to clean cesspools and privies when they become so full as to necessitate emptying, although some municipalities provide that they shall be cleaned out periodically, as once a year, for example. In some English cities, in France, and in many warm countries where the water carriage system of sewerage is not used, special receptacles and collecting wagons are employed and the excrement is taken away at frequent intervals.

As generally done in the United States, the removal of night soil is costly, imperfect, and far from satisfactory from a sanitary standpoint. But with careful supervision it can be carried on with relatively little objection. Barrels and wagons can be made tight and kept clean, the night soil can be excavated without destroying the shrubbery or other property and the material can be finally disposed of by applying it to land. In the cleaning of over 1,000 privies under the direction of the author of this paper there were no complaints from property holders, no illness among the workmen and the material was disposed of, counting all expenses from the privy to the field at about 1 cent per gallon. The material was buried in shallow trenches dug by a plough and at once covered.

The disposal of excrement, in such condition as is likely to be met with in cities and towns which are unprovided with sewerage systems, is an important field for discussion, since the methods to be followed apply practically to all villages and towns and to some extent to most cities. Theoretically the material is highly dangerous, containing, as it often does, the germs of many infectious diseases. Practically it does not appear to be so.

The disposition of night soil offers opportunity for the utilization of the nitrogen and other manurial ingredients of feces which in sewage is highly diluted with water, yet science shows that its value as a fertilizer is not so high as many persons suppose. The custom of the inhabitants of China and some other countries in hoarding their excrement for the purposes of agriculture is thought by some to mean only that these people are very thrifty. Commercial companies which have been organized to turn human excrement into fertilizers for the market have never been successful for long.

The trend of recent effort in the disposal of excrement is toward better-built privies and cesspools and stricter board of health control over the subject and the construction of sewerage systems wherever practicable. It is recognized that flies and other insects must not have access to the material, and that the danger that food and drink may become contaminated by it must be reduced to the lowest terms. Properly managed privies and cesspools may, in certain cases, afford the best means of solving the excrement problem. Sewerage systems are not always either feasible or desirable.

Street cleaning.—Turning now to the subject of street cleaning, another division of our general topic, we find certain standard practices and on the whole a much better stage of development. But even here there is considerable diversity of procedure in the efforts made in different cities for the accomplishment of the same object. It must not be overlooked, however, that the work to be done in cleaning a pavement is not always the same. Different conditions of traffic and of pavement produce different effects. A degree of cleanness which is suitable for one part of a city may not be appropriate at all for another. The best-cared for sections are usually those which are most difficult to keep clean. The most neglected parts of cities are the outlying districts. These often appear to be utterly forgotten by the street cleaning authorities.

In no case should there be unsightly litter, nor the excrement of animals, except for brief periods of time. Dust should be prevented as far as it reasonably can be.

Not that the dust is dangerous so much as because it is disagreeable. Dust is, moreover, costly for householders to remove from their homes and injurious to fabrics and other things.

The trend of modern practice is distinctly toward the prevention of dust, which means the collection of this material either in its familiar dry form or as mud, which it becomes when it is wet. The future to judge by the efforts which are now being made will witness more distinct improvements in this direction than in any other. Machines, as yet of doubtful efficiency, may be developed to operate on the vacuum principle to pick up street dirt and store it in a suitable receptacle until it can be finally disposed of.

Hand and machine work.—There are two general ways of cleaning streets which demand consideration here: hand and machine work. Handwork is the more mobile and effective method and is to be preferred where the pavement is poor or the work difficult for other reasons or the best results are desired. Machine work is to be preferred on the score of economy and speed.

Under handwork is to be mentioned the prompt picking up of litter, including papers, fruit skins, and horse droppings, which, if allowed to remain on the pavement, would invite to a further dirtying of the street and would become ground up and so made more difficult to remove. The labor of this sort which is entailed in most American cities is very large—it is unnecessarily large. A great deal of the dirt in our city streets can and should be prevented by the police enforcements of suitable ordinances. No one should be allowed to throw papers, house sweepings, ashes, or other refuse into the streets. It is forbidden in German cities and it should be equally unlawful elsewhere.

With the best of care some littering is unavoidable and this best can be taken care of by what is known as the orderly, or patrol, or block sytem. In this system men or boys are required to patrol certain districts and pick up the large articles of refuse and place them in suitable receptacles for final removal and disposition. In the United States the receptacles are generally jute or canvas bags conveniently hung on two-wheeled hand carts, or barrel-shaped cans carried in a similar vehicle. When a receptacle is full it is exchanged for an empty one, the full receptacle being temporarily placed where it can be seen and picked up by men with carts especially assigned to that duty. A weak point in this system is the temporary storage. The receptacle may be left too long and in too conspicuous a place. Sometimes the material is not contained in a receptacle, but is simply piled up near the gutter; under such circumstances it is very likely to get scattered about by passing vehicles and by winds.

Sweeping.—The proper function of sweeping is to clean pavements of the finely ground dirt, which is dust when dry and mud when wet. It may be removed in either condition, but from the sanitary standpoint it should never be dealt with by a process which raises the dust into the air. Brooms of special design and of standard form are are usually employed, irrespective of the kind of pavement or the character or amount of dirt to be removed from it. There is room for considerable improvement here.

To prevent the raising of dust when sweeping, it is often customary to sprinkle the pavements; this is usually done by means of a horse-drawn watering cart. Good judgment is required in order to apply the right amount of water, for if too little is used the material is not sufficiently moistened and some of the dust rises into the atmosphere; and if too much is employed, the material is reduced to a condition of plaster which the broom smears over the payment. At best, hand sweeping is expensive, for the labor is arduous and the area which a workman can properly care for is relatively small.

The material which is swept up is commonly stored on the pavement in piles until it can be removed to the place of final disposal in carts. This practice is apparently unavoidable. It is least objectionable when the dirt is collected promptly. When

the piles are allowed to remain long, a considerable amount of the dirt may become scattered upon the pavements again by the wind and movements of vehicles.

A substitute for hand sweeping lies in the use of the revolving broom attached to a suitable frame and drawn by one or more horses. Many cities use the horse broom and it may be said to be a standard piece of apparatus. It should always be preceded by a sprinkling wagon when the material to be removed is not already damp. It could be used to great advantage during and immediately after rain, but it seldom makes its appearance under such circumstances. In some cities where there is a great deal of work to be done, horse brooms travel in gangs, the broom being so adjusted as to throw the dirt to one side, each broom taking it up where the other left it and carrying it nearer and nearer to the side of the street, until it reaches the gutter. Here the dirt is shoveled into piles to be collected into carts for final disposition.

Flushing.—The most recent advance in street cleaning lies in the use of a stream of water to cleanse the pavements. The object is to secure a greater degree of cleanness than is possible with broom work. This method is commonly called flushing, but it is not merely flushing. When properly done, the stream sweeps as well as flushes the material away. Before the water is applied, the material to be removed should be thoroughly lubricated to remove its adhesiveness toward the pavement. This is best done by means of sprinkling wagons which thoroughly wet the pavements before the water is used to carry the material to the gutters.

Street flushing is sometimes done by means of a fire hose and sometimes with wagons which carry a supply of water and direct it downward under pressure upon the pavements. Under favorable circumstances, good results can be obtained by either method, but where the pavements are irregular, very dirty or the smallest quantity of water must be used or the cleanest results obtained, no automatic apparatus can take the place of intelligent and experienced hand workers.

It is often feasible and desirable to scrub or scrape the pavements with brooms or rubber squegees. These tools may be used in the hand or operated mechanically. An automatic scraper which is equipped with rubber placed spirally upon a horizontal drum has been found to be one of the most serviceable pieces of equipment for this service. Like flushing, it was first used extensively in Europe.

It is perhaps unnecessary to point out that in selecting the method to employ in any case, the choice should depend not alone upon the results which are obtainable elsewhere, but under the particular conditions with which one has to deal. Before any system of water cleansing or sweeping is decided on as the best for any case, it will be desirable to consider it in all its local aspects. Experiments and tests of appliances and methods may be exceedingly helpful.

Combinations of apparatus have been invented for sweeping, sprinkling, picking up dust and carting it away, and very large pieces of apparatus have been built to clean streets on the vacuum principle. There are many difficulties in the way of successful machines of these types and it does not appear that they have all been overcome. One of the main obstacles is the irregularity in the surface of the pavement, another is the variety in the consistency of the dirt to be removed. In time, perhaps, such automatic apparatus will largely supersede hand work, but that time has not yet arrived, except in some cities where the conditions are decidedly favorable.

Final disposition of street dirt.—As to the disposition which can be made of street dirt, it is well to consider that the main object should be to get rid of the material in a sanitary way, and attempts to extract the manurial values present should be a secondary consideration.

The manurial value of street sweepings is less than it would be if the material did not lie our in the wet and air and become mixed with useless dust. The fresh horse droppings have the most value, and it is often more economical not to attempt to use them than to gather them with the idea of putting them to practical use. When horse droppings are collected promptly and removed, the pavements are to that

extent protected from objectionable littering, but this work should be done for the sake of cleanness, rather than for profit. Sometimes street sweepings are placed in piles and allowed to ferment like compost. This is an admirable procedure when the opportunities are favorable to it, but the resulting compound is not of much value.

Snow.—The removal of snow is one of the most costly and unsatisfactory branches of street cleaning for the reason that the amount of work involved, if large areas of pavement are cleared, is very large and its occurrence uncertain and irregular. Most cities do little to clear away snow except upon the main highways, and there are few, indeed, where even this result is accomplished to the general satisfaction. For the most part cities allow the snow to lie upon the pavements until warmer weather occurs, when the compacted mass is picked and broken and the natural melting facilitated.

Like the disposal of refuse generally, the removal of snow involves three processes: 1, Collection; 2, carting; and 3, final disposition. For collection the main reliance is hand labor, shovels, and sometimes when the snow is compact and frozen, picks being the tools most often employed.

It is customary to shovel the snow into piles located at convenient distances apart at the center or sides of the carriageways. Carts and wagons of the largest capacity available are then driven alongside and the snow is shoveled into them. The carts are hauled to dumping places which should be as accessible as possible, rivers, parks, and empty lots often being utilized.

Recent improvements in snow removal have been made by the employment of plows to assist in the collection and in the use of sewers as the place of final disposition. It has been found that large sewers are capable of carrying off a great deal of snow without injury to them, provided little else than snow is put into them. Following European custom, great improvement has been made in perfecting the organization necessary to handle the snow. The largest item of expense being in the labor employed, and this labor being necessarily of the poorest sort, an improvement in the organization of the directing force of permanent employees which helps to direct the auxiliary laborers, makes for efficiency and economy.

In future the work of removing snow is likely to see considerable improvement in the organization of the workers, in the use of the sewers and in the apparatus designed to supplement the large amount of hand labor which must always be the chief reliance. The use of salt to melt the snow and the employment of streams of flushing water to carry the snow into the gutters and sewers appear to offer some promise in those situations wherein the cold is not excessive and the water is available at no great expense.

II. SEWAGE DISPOSAL.

According to statistical information, it appears that most of the cities of the United States are provided with sewers, to some extent, at least, but have no means of getting rid of their sewage, except by discharging it into a natural body of water in the vicinity. As sewers first came into use for the means which they afforded for carrying away rain water from the streets, so they are likely to be built in the small and growing municipality for the same purpose to-day. There is, perhaps, little objection to be raised against the discharge of surface water to the rivers, but when house sewage and the drainage of factories are added, grave consequences may, and often do, follow. These consequences are of two general kinds—danger of disease and risk of nuisance. The nuisance may be an offense to the sense of sight or smell. The danger of disease is usually through the pollution of drinking water; but it must not be forgotten that a nuisance may have a prejudicial effect upon health, so that the line separating the two clases of objectionable consequences just drawn, should not be regarded as a very sharp one.

Extent of treatment required.—Many sanitarians have contended that the proper function of sewage disposal works was to prevent nuisance only, and that the proper

way to protect a community from polluted rivers and other natural bodies of water, was to avoid the use of the unpurified water for drinking purposes. Their contention has been that the streams were natural sewers and should be utilized as such; that it was cheaper to purify the drinking water supplies than to keep all natural bodies of water clean enough for domestic uses without purification. It has been argued that the only practicable way to deal with the problem of utilizing the rivers and lakes for sewage disposal and water supply is to let the sewage into them and regard all water obtained from surface sources as polluted and requiring to be filtered or otherwise rendered suitably pure.

This is the status of the subject in the United States to-day.

Sewage should be discharged only in such quantity and in such places as will not produce a nuisance and add unreasonably to the difficulty and cost of purifying the water for such purposes as it may be required to serve. Nearly all drinking water supplies, unless from underground sources, must be regarded as probably unsafe unless artificially purified. This point of view should be kept in mind in considering the methods which are available for the treatment of sewage. By treatment is meant partial purification.

Exhaustive experiments as well as experience in Europe and America have yielded a great deal of information concerning the methods which can be successfully employed for the purpose of relieving sewage of its offensive ingredients, and there is little doubt but that marked progress will continue to be made in this important field for some time to come.

Objects which can be accomplished.—Few sanitary subjects are so complicated or require so varied a knowledge of science for their mastery as sewage disposal; but once the principles of the art are understood, it will be possible to proceed with considerable confidence to the construction of the necessary works. The most successful works are those in which the proper principles are best applied to the local conditions; no single process of sewage disposal exists which is capable of dealing satisfactorily with all cases. Sewage varies in composition and is not of the same volume or quality in different cities or different sewers in one city, or at different times of day in a given sewer. The state of the weather, the season of the year, the character of the district with respect to residence and business occupancy, the nationality and habits of the population and other conditions all affect the quality and quantity produced. Standard methods of treatment exist, but they apply only to standard conditions. The success of a system of sewage treatment depends upon the completeness with which it is suited to the particular situation to be dealt with. To many persons the repetition of this fact may seem unnecessary, and yet it is to its continual neglect that most of the failures in the works which have been built are attributable.

The best methods for the treatment of sewage have for their immediate objects the removal of the grit and other relatively large and solid matters, the destruction or abstraction of the very finely divided colloidal and other semisolid substances, and the oxidation of the remaining liquids.

The processes may be said to be mechanical and biological and chemical, according to the principles upon which they operate. The mechanical methods aim to remove the relatively large solids and some of the colloids. The biological undertake to destroy the peculiar molecular structure of the colloids which are not removed mechanically and to carry on the oxidizing processes. The chemical procedures aid the mechanical and biological effects and sterilize the sewage when that extreme measure is attempted. No one of these processes is capable of adequately treating a sewage except where a partial and imperfect effect is desired. It is usual to employ two or more, each to do a certain share toward the general result desired.

MECHANICAL PROCESSES.

a. Screens and grit chambers.—Mechanical methods include grit chambers, which are essentially enlargements of the sewer as it enters the disposal plant. As the

sewage flows into the chamber the velocity of the current is retarded and this slowing causes the solid matters to settle out. Facilities are provided in the form, often, of dredging machinery, for removing the grit from the bottom.

In connection with the grit basins, there are generally coarse screens composed of heavy bars placed an inch or more apart, for the purpose of intercepting large floating substances.

Fine screens are sometimes used to take out of the sewage the solid matters which are not heavy enough to sink readily in the grit chambers. If not removed, these solids become more and more comminuted and add materially to the difficulty with which the more refined processes of treatment can be carried on. The fineness of these screens and the ingenuity with which they are constructed, are among the most recent advances which have been made in the whole art of sewage treatment. The best screens are so constructed as to present always a free and clean surface to the sewage stream. This result is accomplished by means of machinery which carries the screening surface slowly up out of the sewage and there cleanses it before the screen automatically revolves back for a new load of solid matters.

Fine screens have reached their highest development in Germany. England, which leads the world in nearly all other branches of sewage treatment, possesses but few examples of fine screens. The Germany screens are standard for Germany; nearly every large city is provided with them in some form. The forms are various; it is possible to find one to suit almost any requirement. The difficulty is to know which is the best for the particularly case in hand, and just what to expect of it under American conditions. Again, being of complicated construction, it would seem necessary to employ a considerable amount of skill to operate one successfully. But this objection is rather a general one and can not be escaped in sewage disposal. No process is capable of good work without good attention.

Between the complicated fine screens of the Germans and the common bar screens which are a necessary feature of all works lies a large variety of screens of varying degrees of efficiency. Their function is to collect such relatively large substances as leaves, matches, cloths, paper refuse, and whatever else will gather upon them. Screens of these kinds are often employed and are generally inefficient, being poorly provided with cleaning arrangements and too coarse to gather much material.

The screenings are disposed of in different ways, according to their amount, and the natural aptitude of the people to turn such material to account. In Germany the screenings are often used as manure, sometimes they are burnt. In all cases they are exceedingly offensive, and should not be stored or handled any more than is absolutely necessary.

b. Settling basins.—Settling basins are regarded as one of the most useful, as they are one of the most frequently met with devices used for the treatment of sewage. They are of various types and perform various functions, although their chief usefulness has, until recently, been considered to lie in the removal of solids which will subside if given a chance to do so.

In its simplest form a settling basin is a tank of such size as to permit the sewage to flow slowly through it in about three or four hours. The bottom slopes gradually toward a large outlet pipe which is used when the solid matters are cleaned out. An inlet and an outlet for the sewage are provided at opposite ends of the tanks near the surface of the liquid. The solids are deposited as the sewage flows through the basin or is allowed to stand quiescent in it, according to the method by which the operation is conducted. Sometimes chemicals, such, for example, as lime and iron, are applied to the sewage to increase and hasten the settlement; this method is termed chemical precipitation. It is not so much used now as formerly.

Improvements have been made in the settling basin just described until its original functions, as well as its appearance, to-day are scarcely recognizable. Among the most interesting and important of these changes were those which were brought about

by the discovery that if sewage was kept in a settling tank for a period of eight hours or more it would putrefy and much of the solid matters which gathered upon the bottom would become liquid, thereby lessening the frequency with which the tank would have to be emptied of its sewage and the accumulations at the bottom removed. This new process was thought capable of affording a nearly complete solution of the sewage problem, for it promised to do away with the troublesome question of disposing of the settlings. A settling basin operating upon the principle just indicated was called a septic tank. At first the limitations of the septic tank were not recognized. To-day it is probable that no engineer would build a septic tank for large works, even in connection with other devices, except under unusual circumstances.

The latest development in settling basins is the Emscher tank, the invention of Karl Imhof, of the Emscher drainage district of Germany. The Imhof tank possesses two notable features: First, great depth and a pointed bottom, which causes the depositing solids to settle toward an outlet pipe, from which they can be withdrawn without emptying the tank of its sewage. Second, a trap through which the solids settle to a bottom compartment and from which they can not escape to the flowing sewage above. The sewage passes through the tank too rapidly to become foul, as it does in the old septic tank, but the solids imprisoned in the trap remain long enough to undergo a complete fermentation with a result which is truly remarkable. Whereas the accumulations at the bottom of an ordinary settling tank consist of a very watery mud which can be dried only with great difficulty, the material drawn from the lower part of the Imhof tank quickly parts with its water on standing. It can then be burnt or used for filling low lying land. Immense volumes of inoffensive gas are produced in the process, and the solids taken out are relatively small in volume and practically inodorous. Hundreds of new tanks have been built on this principle within the last few years, and many sewage works formerly employing plain sedimentation or septic tanks have been constructed on the Imhof principle.

Processes of oxidation.—When sewage has been deprived of its settleable solids by sedimentation of some kind or the solid matters have been removed as far as possible by screening, it is still capable of producing offensive odors in rivers and other natural bodies of water unless the diluting power of the latter is large, and for this reason some further process of treatment frequently becomes necessary. The odors are due to putrefaction, or, in other words, bacterial fermentation in the absence of oxygen. Experience has shown that in the presence of a proper supply of oxygen, objectionable odors will not be produced. The organic matters which are a characteristic of sewage become oxidized and so converted into mineral compounds which are inoffensive and incapable of becoming so.

It has been found practicable to cause the oxidizing changes to take place in artificially prepared beds of broken stone or other solid media through which the sewage is allowed to pass very slowly with an abundant supply of atmospheric air. Sometimes the beds are contained in water-tight basins and the sewage is allowed to flow into them, remain in contact with the stone for a period of two hours or so, and then drawn off; in this case the device is called a contact bed. More often the beds are built upon an impervious floor without containing sides. The sewage is sprinkled over the top of the stones and allowed to drain slowly through to the bottom; in this case the beds are known as sprinkling filters or percolating filters. Both contact beds and sprinkling filters are capable of doing excellent work, but the latter are by far the more effective for a given amount of land. Large works on each principle exist and have proved effective even in cold climates.

The oxidation, like the putrefaction of sewage, is brought about by the activities of special types of bacteria, and it is by providing the suitable conditions for their life processes that the desired results are secured. When suitable conditions for the particular kind of bacterial action desired are not provided, the whole process fails. Thus, oxidizing beds are able to take care of a definite amount of sewage stuff per acre

and will handle no more. If more be added, or the supply of atmospheric oxygen be diminished, the bed becomes sick and the improvement in the sewage stops.

The latest advance in sewage-disposal practice has been accomplished by doing away with the stone beds and giving the oxidizing bacteria their proper supply of oxygen directly by pumping air through the sewage. This process can apparently be carried on in tanks like the old-fashioned settling tanks, if necessary. Experiments made at the famous sewage testing station at Lawrence, Mass., at Milwaukee, Wis., Manchester, England, and elsewhere, give promise of a substantial advance in the efficiency, reliability, and economy with which sewage can be treated in this general way.

Utilization of the manurial value of sewage.—There was a time when it was thought that the manurial value of sewage should serve as an incentive for the employment of this kind of municipal waste as fertilizer. Economists solemnly warned the public that millions of tons of nitrogen were being wantonly thrown into the watercourses when the world's supply of guano was showing signs of depletion. It was claimed that the heedless pursuit of this policy was certain to result disastrously in course of time. The sewage should be returned to the soil.

Under mistaken ideas of conservancy attempts were made to apply sewage to agriculture, and these efforts were persisted in in England until the subject was thoroughly tried out. There are now some large farms using sewage, not only in England, but on the Continent of Europe. But it is no exaggeration to say that there is hardly a city which would not willingly give up its sewage farms for more modern and intensive methods of disposal if it could do so without sacrificing the money which is invested in the existing works. Sewage farming affords a good way to get rid of sewage providing the climate, soil, and agricultural conditions are favorable; but it can rarely be recommended unless the water, aside from the manurial ingredients, is needed for the crops.

Such fertilizing value as sewage contains is difficult to turn to practical account. For one thing, the useful materials are too highly diluted; sewage, as ordinarily produced by the cities of the United States, is about 998 parts water to but two parts of solids, and of these two parts, only one-half is organic matter. Ordinarily, land does not require, nor can it take, a great deal of water at all times, and yet the sewage must be gotten rid of at times of rain and frost and in the unproductive period. Furthermore, it has been abundantly shown by competent agricultural chemists, that such fertilizing values as are present are not, for the most part, in available form for plant food.

The most promising way in which sewage matters can be utilized for the manuring of crops is in the form of a dry powder produced from the sludge of settling basins. Filter presses and other drying apparatus can be employed to get rid of the water, but the undertaking is expensive. Some fertilizer is made in this way; the amount is not large. Up to the present time it has cost too much to separate the useful materials from the water. The subject, in spite of the interest which has been taken in it for more than a generation, still lacks practical development.

Sludge.—In most sewage-disposal works a great deal of mud or sludge, as it is called, is produced, and the final disposition of this material offers many difficulties. Some cities carry it to sea and dump it from steam vessels constructed for the purpose; others discharge it into lagoons where it lies, an unsightly and malodorous mass, for long periods of time until the forces of nature eventually consume it. In order to avoid the insanitary conditions which sewage produces when discharged upon land, it is often ploughed into the soil. In Germany centrifugal machines are used to express a part of the moisture, after which the sludge is further dried by heat and burned. There are plants in England and America where the material is passed through filter presses and then dumped upon low-lying land.

Recently it has been found that sludge will ferment, if kept stirred up and mixed in certain ways with fresh and stale material, and after this change takes place the water

will easily drain away. This is the secret of the Imhof tank—the Dickson and activated sludge processes and other methods more or less resemble them.

In some cases where the sewage is particularly rich in useful ingredients, special processes are employed to recover the useful materials. Thus, grease can profitably be recovered in certain cases. We are here approaching the field of the industrial chemist. Corporations which think that their wastes contain valuable substances which it is shrewd business policy to recover, are often compelled to employ chemical ability to work out the best system of utilization.

Various trades produce peculiarly offensive liquid discharges, as, for example, gas making, paper making, leather tanning, wool scouring, and brewing. Much experience has been gained, particularly in England, in utilizing industrial wastes, or at least, in ridding them of their offensive character, and the steps which should be taken in disposing of them are still the subject of continuous study. Speaking broadly, the underlying principles for the disposal of trade wastes are much like those which have been described in this paper for the disposal of municipal wastes. Screening, filtering, settling, precipitating by means of chemicals, biological treatment, application to land, filter pressing, dumping, burning, and discharge into natural bodies of water are all practiced.

Literature.—The literature of the subject of waste disposal is large and scattered through the textbooks and journals of various sciences and professions. There is no comprehensive work which deals adequately with all branches of the subject. The richest literature is that of sewage disposal; the poorest is that which relates to the solid wastes. England and Germany have been the greatest contributors, although America is conceded to have produced much of incalculable value.

A feature of American effort has been the making of exhaustive investigations and the publication of correspondingly elaborate reports concerning the disposal of the sewage of particular cities. Of special interest are the reports which deal with the sewage of New York, Chicago, Philadelphia, Boston, Baltimore, Worcester, Columbus, Milwaukee, Pittsburgh, Gloversville, and Cleveland. The researches of the Lawrence Experiment Station of the Massachusetts State Board of Health into the disposal of sewage and the purification of water are classic.

In England the reports of the Royal Commission on Sewage Disposal, which was appointed in 1898 and continued until 1915, easily overshadow all other work of this character in the scope and practical aspects of the subjects dealt with. Many English cities have also issued reports of the utmost value with respect to their sewage disposal problems; as, for example, London, Birmingham, Manchester, Leeds, Sheffield, Salford, and Bradford. The reports of the English rivers boards are interesting and instructive. The reports of the Rivers Pollution Commission, the Health of Towns Commission, and similar bodies are regarded as having laid the foundation for much of the best work which has been done in all countries in the disposal of sewage. In Germany the reports of the Imperial Sewage and Water Testing Station, whose headquarters are in Berlin, and the reports of the cities of Berlin, Frankfort, Hamburg, Dresden, Cologne, and many smaller places are among the most useful by way of reference.

With regard to the disposal of solid wastes, intersting information may be found in reports issued by the cities of Boston, New York, Philadelphia, Chicago, Baltimore, Milwaukee, and Cleveland.

The periodical literature is far too large to mention in detail. The student should consult the proceedings of engineering societies and chemical associations especially, and give careful attention to the engineering trade papers for descriptions of the most recent developments in sewage and solid waste disposal. Best of all, in order to get a comprehensive knowledge of the subject, will be a tour of inspection of some of the great cities where disposal works are in operation and where opportunity may be given to meet the splendidly trained and intelligent men under whom, in many cases, the disposal works have been constructed and to whose intelligent efforts further progress is to be looked for.

The CHAIRMAN. We have papers on this same subject by Prof. William T. Sedgwick, of the Massachusetts Institute of Technology, and Mr. J. T. Fetherston, commissioner of street cleaning, New York City. I shall now call for their papers.

DISPOSAL OF REFUSE.

By WILLIAM T. SEDGWICK,
Massachusetts Institute of Technology.

We are all creatures of fashion, followers of fashion in sanitation as well as other matters, but I am inclined to think that the pendulum has swung too far. We can not say in sanitary matters, as we may in the law, "De minimis curat non lex." The law does look after the least things in sanitation, and will forever look after the least things, because as we go along we are getting the big things looked out for and have to attend to the little things. At any rate, cleanliness will always be the mother of sanitation and hygiene; and in dealing with these wastes, sewage, garbage, street dirt, and all the rest, we are dealing with fundamentals of cleanliness, and if we ever take the standpoint, as some people are taking to-day, rashly and without thinking, that boards of health have nothing to do with such things as garbage disposal and the disposal of street dust and the like, because they at the moment have so much more to do with infection and epidemics, then we shall make a very serious mistake, and boards of health will find themselves by and by having a certain amount of disease from sources which they had overlooked. The sanitary chain is no stronger than its weakest link, and we have got to pay attention to all these things.

Now, Dr. Soper began with night soil, and the proper disposal of night soil is a very serious matter. If it is put on cultivated fields for lettuce and cabbage and the like to grow upon, if men track it on their boots, or chickens carry it on their feet to open wells, then it becomes a serious sanitary menace. In rural sanitation the disposal of night soil is the principal problem. In the public health service here, Dr. Lumsden is showing some wonderful results that he has accomplished in rural sanitation in several of the counties of West Virginia and Maryland and Indiana and Kansas—marvellous reductions of typhoid fever, largely by attention to the proper disposal of night soil.

While in a large and engineering way, the board of health may be said to have very little to do with the disposal of night soil, to take very little interest in it in some cases, in other cases it is going to be the principal work of the future. The invention and the stimulation of the use of sanitary privies is one of the most important subjects of the time. There is one at the hygienic laboratory now, a model sanitary privy, which everybody who is interested in rural sanitation or in tropical sanitation, where the privy is wanting or too rare, should get acquainted with. It is a most interesting development.

Again, touching on a matter which is not always thought of, there is the sanitary disposal of sewage on steamboats and railroads. The sanitary disposal of the waste from these sources is sometimes a serious matter. For instance, when steamers leave the Chicago River and go out near the intake of the Chicago water supply, great excursion steamers laden with thousands of people, and the discharges from the closets go into the lake near the intake, it can not help being a serious thing. Just how serious the scattered disposal from a moving train is or is not, no one knows; but, as you know, closets are still locked upon trains in certain parts of the country passing over certain watersheds, and while that is a barbarous method and in some respects absolutely to be disapproved of, it is better than none. From the standpoint of personal hygiene,

from the standpoint of efficiency, it is all wrong; but it is better than allowing the excreta to go into a public water supply over which a train may be passing. Within my own knowledge, I have known of two instances in which human excrement from passing railway trains was found right in a public water supply and not far from the intake.

The question of stable manure is an important one because of its connection with vault building and flies, and the health officer of Brookline, a town in which I have been living for some time, is proposed to take municipal charge of this matter and have municipal disposal for a more satisfactory sanitary treatment and control of the vault nuisance.

I can confirm, and heartily confirm, Dr. Soper's statement of the inefficiency of many street "squeegees." They simply pass over the dirt, allowing it to dry and blow about. I have had my mouth partially filled with pulverized horse dung and other refuse for so many years that I hope I am immune, but it is not pleasant. Boston, for instance, in a windy time, has an atmosphere of pulverized horse dung and other dirt, although these "squeegees" are used there very frequently. Anyone who has seen the street washing in Munich and then watched it in any of our American cities has noticed the difference; there it is efficient, here it is generally very inefficient. And let me say that I heartily second Dr. Soper's suggestion that we hear from our Central and South American friends in regard to their sanitary efforts in these various directions, for we need to know more about their ways than we do.

When we come to garbage, we have again a variety of connections between sanitation and engineering. From the moment the garbage leaves the kitchen until it is either destroyed by burning or by reduction or by hogs or something else, it is a nuisance and a certain source of danger; probably not a source anywhere near as important as sewage or some other things, but still important. The handling of garbage, for example, from tenement-house districts in which a variety of diseases may be existent, is liable to infect the handlers; and even if no infectious disease is carried by it the nuisance which arises from the carting of the garbage through the streets by those that generally do it is unpleasant and needless except under our system—apparently it is necessary there.

Then, the garbage pail in the back yard, or the garbage can, is a source of trouble. Dogs and cats and rats by day and by night scatter things about, and if the rat problem is a serious one, as it always should be regarded, then the garbage can is a most important sanitary appliance. I have often smiled when I have observed that the able and highly trained officials of the United States Public Health Service have sometimes descended from their lofty level to invent and approve garbage cans. The modern medical man is so far descended from Æsculapius that he is now inventing and approving garbage cans; and I rejoice in this fact, for it shows that he is getting right down to mother earth and doing fundamental things. When, however, he goes further and invents a new word, "deratization," the philologists may have occasion to quarrel with him but I certainly shall not. The vermin that gather around the garbage pail and make the back of the house a nuisance are not only objectionable from a sanitary point of view, but in time of plague become very dangerous; unpleasant always, dangerous occasionally, and yet back doors are neglected in your house and in my house. As a rule we do not pay much attention to the back door, however much we pay to the front.

As to the sanitary aspects of garbage reduction and incineration and the like, so long as no public nuisance is produced, I see on objection to any of these, excepting the hog disposal method. It has been found that hogs in municipal piggeries are often very tuberculous, and that is, of course, a serious matter. Moreover, piggeries for the disposal of public refuse are almost always public nuisances, because the hog is not a sweet-smelling animal under any circumstances. Municipal piggeries

have been proposed, but I do not think that the idea will bear serious consideration because of its nuisance features.

Garbage-reduction plants are often a nuisance, because of the odors they produce, and public comfort must go with public safety. The interpretation of public welfare, which brings sanitation close together with comfort, is too often overlooked.

In this connection, and in connection with sewage and its sanitary aspects which are so well known to us all, I want to say there is one thing in this country which is, at any rate, fearfully neglected, and that is the establishment of public-comfort stations. In an address at Rochester two or three months ago I remarked that the most flagrant failure in American sanitation to-day is the almost universal lack of public convenience or comfort stations in American cities or towns. Now, this is a sanitary matter connected with the disposal of personal sewage and it is bringing the thing down to the very bottom. The stranger within the gates of most American communities seeks in vain for any public sanitary conveniences. If he is well dressed he must be referred to hotels or other semipublic buildings; if poorly dressed, to saloons or railroad stations or other semiprivate or public-service stations. In sending out my abstract to the authorities of the Rochester meeting I wrote, as I have just read, "the most flagrant fai'ure;" but I was in despair to find on arriving that it had been sent out to the press all over the country as "the most fragrant failure," and I am afraid that that was quite as correct as the other, because one of my students came to me the other day and said, "Professor, I thought that Boston was a leader in sanitary matters, but if there is a worse smelling place than that comfort station down on the Common I would have to go far to find it."

It turned out a little later, on investigation by Dr. Wilbur, of the New York State Board of Health, that in Madison Square, New York, through which, as you know, tens of thousands of people pass every day there is no public comfort-station. They had one about a year ago, but it was so filthy that they decided to close it up. That, I think, bears out what I have been saying, that the most flagrant failure in American sanitation to-day is this matter of the failure to provide public-comfort stations, and I may say here, by way of parentheses, that Dr. Wilbur was so much stirred up by this discovery of his in New York, as well as by my remarks, that he has established a league for the enforcement of the common decencies of life, which is to be known as the "Public Comfort League." This is one of the most remarkable things that I ever heard of, for the constitution provides that there shall be no officers, rules, regulations, annual meetings, or dues. Any person may become a member at any time, at any place, by helping along, etc. You see what an admirable thing this is, such a league as we have always been looking for, having no meetings, no officers, no dues.

Now, beginning with the disposal of personal sewage in comfort stations and elsewhere, we come to these methods of which Dr. Soper has spoken so well and of which Mr. Featherston will have much to say, no doubt, although his subject is more particularly the garbage and the street work. We do not need to dwell on the need of the disposal of sewage. That has been proved too often by epidemics and in sanitary science. I may say that at a sanitary laboratory, of which I am director, we have been experimenting on a method for the treatment of sewage by sulphurous acid, with recovery from the sludge of grease, and to our surprise have found it much better than we had supposed, so I think I may say here, and I think it will interest all the sewerage people as being somewhat new, that there is a possibility—I can not say any more than that—that a process not too costly and perhaps even slightly remunerative may be devised in the near future, by which domestic sewage and certain trade wastes may be treated by sulphur, in this case preferably sulphurous acid, causing a precipitation of a sludge rich in grease, rich for sewage. From that the supernatant liquid can flow off, practically sterile and reasonably clear, so that it may be poured into a harbor or lake or stream with little sanitary danger. The proc-

ess, then, involves the extraction of a specially precipitated sludge for the grease which it has, and at the moment it looks as if the process might be successful. I do not want to say much about it, because we are always wary about these new processes and we have had so many failures that we do not want to risk another, but careful and repeated experiments which have lately been made in the little laboratory, of which I have had the direction, upon Boston sewage and on a reasonable scale have led us to the point where we want to make experiments on a large scale and intend to do it if we possibly can.

Anything which would thus sterilize the greater part of the liquid of sewage and then leave us to deal with a sludge economically valuable would be a very great boon. We may not have reached this, but we are certainly working in that direction.

So, from the sanitary point of view, I want, first, in the way of recapitulation, to protest against the current idea in some sanitary, and more particularly medical, circles and boards of health that these questions of sewage disposal and garbage disposal and street cleaning and the rest are not sanitary questions, that they are not to be regarded within the natural purview of boards of health. That is a temporary fashion which must pass. I have explained the reason for it. The law of sanitation must take account even of the least things and of the most remote things dealing with the public health, and we must give attention to the sanitary aspects of garbage disposal, of street cleaning, of sewage disposal, and of all the other branches of waste disposal. Of course if we could burn everything up economically, or even at a small loss, it would be well to do so, provided it could be done without producing a nuisance, but at present in most cities that does not seem to be practicable. On the other hand, principles of conservation make us wish to get what we can out of these wastes. If a ton of garbage will keep 75 hogs a day and turn them into food for man, that is a very taking proposition on the face of it, and that is said to be the case; but if the keeping of the hogs produces a public nuisance and exposes a lot of people associated with the hogs and with the garbage to the contracting of infectious diseases, then it is a great deal better to burn the stuff up and get rid of it even at a loss. We must never lose sight of the sanitary side of the case, although it is the engineering side that is always put first because of the economies of the problem.

COLLECTION AND DISPOSAL OF MUNICIPAL REFUSE.

By J. T. FETHERSTON,

Commissioner of Street Cleaning of City of New York.

The topics discussed in this paper will be restricted to the consideration of (1) the quantity, quality, and seasonal variations of household wastes and street sweepings, and (2) the cost of collecting and disposing of these classes of refuse.

Household refuse consists of ashes from furnaces or heating appliances, garbage or organic wastes resulting from the preparation or use of foodstuffs, and rubbish or articles from households not comprised under the terms ashes or garbage. Street sweepings consist of miscellaneous materials removed from public thoroughfares.

For any particular municipality there is one most suitable, sanitary, and economical method for the collection and disposal of refuse, and any approach toward a satisfactory solution of refuse handling can only be attained by a detailed study of all local conditions bearing on the problem. Scientific data on the subject until recent years have been, and even to-day are, generally unsatisfactory. For any city it is almost hopeless to expect a satisfactory solution of the collection and disposal question unless

the amount, character, and variations of refuse materials are definitely known for a period or cycle of at least one year. With such data the next step usually is to secure information from and study the practice of other cities, and the results therein secured. In all cases sanitary efficiency should receive primary attention, and cost or expense should receive secondary consideration. More often than not these items are considered in reverse order.

The collection and disposal of refuse from a sanitary standpoint involves to a greater degree the comfort and convenience of citizens rather than the actual health aspects of the community, though it is true that garbage affords a breeding place for flies; dust from ashes affects the respiratory organs, while rubbish may contain discarded materials from the sick room, carrying pathogenic organisms.

From the cost standpoint it is apparent that the enormous volume of waste produced in municipalities and the great cost of collection and disposal of refuse should be more forcibly brought to the attention of citizens generally. There are in the United States 184 cities of over 30,000 population, aggregating 27,316,000 people. The expenditures for the collection and disposal of household refuse approximate 50 cents per capita per annum. Thus the total expenditure of $13,658,000 per year gives a clue to the cost of work in the larger cities of the United States.

Local conditions, such as the character of inhabitants, geographical location, and and the nature and amount of food, fuel, and accessories necessary for urban dwellers, determine to a great extent the volume of refuse produced per capita per annum. Statistics from six cities in the United States and one in Canada show an average production of 1,361 cubic yards of household refuse per 1,000 of population per year. (See table No. 1.)

Comparing the foregoing statistics with similar information secured from cities on the continent of Europe, it is shown in Table No. 2 that American cities produce about 2.7 times more household refuse per capita per year than foreign cities. (See Table No. 2.)

The foregoing tables indicate the necessity for discriminating in methods of refuse collection and disposal on the basis of the volume of materials produced, not considering at all the nature or variations in the materials themselves.

For the purpose of securing a comparison by weight of refuse in foreign and American cities Tables Nos. 3 and 4 have been compiled, and here also American cities are shown to produce about twice the amount of material discarded in foreign cities. The difference between weight and volume, comparing foreign with American cities, is undoubtedly due to the greater amount and lower weight of rubbish discarded in American households.

TABLE I.—*Household refuse, volume per annum, seven American cities, 1913.*

	Population.	Number of collectors.	Refuse collected per year.	Population per collector.	Refuse per collector per annum.	Cubic yards of refuse per 1,000 population per annum.
			Cubic yds.		*Cu. yds.*	
New York: Manhattan, Brooklyn, Bronx	5,118,283	1,878	7,429,858	2,725	3,956	1,452
Washington, D. C.	353,297	240	440,368	1,472	1,834	1,244
Boston, Mass.	729,072	656	956,570	1,111	1,458	1,311
Toronto, Ontario, Canada	475,575	361	845,903	1,248	2,220	1,780
New Orleans, La.	373,090	180	509,689	2,072	3,831	1,366
Baltimore, Md.	558,485	197	647,951	2,835	3,288	1,160
Philadelphia, Pa.	1,650,000	600	2,004,000	2,750	3,340	1,214
Average				2,030	2,704	1,361

TABLE 2.—*Household refuse, volume per annum, seven European cities, 1912.*

	Population.	Number of collectors.	Refuse collected per year.	Population per collector.	Refuse per collector per annum.	Cubic yards of refuse per 1,000 population per annum.
			Cubic yds.		*Cu. yds.*	
Hamburg	976,000	.....	414,011	.....	.....	424.2
Nurnberg	360,000	111	125,931	3,243	1,135	349.8
Cologne	516,000	70	232,824	7,371	3,326	451.2
Dusseldorf	380,000	150	175,272	2,533	1,168	461.2
Barmen	150,000	28	52,320	5,393	1,869	348.8
Berlin	2,090,000	400	1,700,400	5,225	4,251	813.6
Paris	2,846,986	750	1,974,130	3,796	2,632	693.4
Average	.....	.....	.....	3,752	2,397	506.2

TABLE 3.—*Household refuse, per capita per annum, by weight, 10 European cities, 1912.*

	Population.	Tons mixed household refuse per annum.[1]	Pounds refuse per capita per annum.
Hamburg	976,000	248,406	509
Nurnberg	360,000	75,558	419
Cologne	516,000	139,694	541
Dusseldorf	380,000	105,163	553
Barmen	150,000	31,392	418
Berlin	2,090,000	1,020,200	976
Paris	2,846,986	1,006,806	707
Finsbury Borough, London	87,923	20,403	459
Manchester	731,677	168,245	461
Sheffield	471,662	121,103	513
Average	.....	.....	550.6

[1] Weight of mixed household refuse assumed to be 1,200 pounds per cubic yard.

TABLE 4.—*Household refuse, pounds per capita per annum.*

	Pounds per capita per annum.				Remarks.
	Garbage.	Ashes.	Rubbish.	Total.	
New York:					
Manhattan	217	1,327	108	1,652	New York Commission on Street Cleaning, 1907.
Brooklyn	145	496	88	729	Do.
Bronx	119	708	51	878	Do.
Philadelphia	109	1,112	72	1,293	Municipal Journal, Nov. 11, 1915.
Boston	235	1,529	43	1,807	X. H. Goodnough (computed.)
Milwaukee	220	476	193	889	Rudolph Hering, 1907.
Buffalo	137	560	120	817	Municipal Journal, Nov. 11, 1915.
Average	169	887	169	1,152	

TABLE No. 5.—*Street sweepings removed, per unit of pavement, per year, European cities.*

	Length of streets.	Area of streets.	Street sweepings, per annum.	Street sweepings, per 1,000 square yards pavement, per annum.
	Miles.	*Sq. yards.*	*Cubic yards.*	*Cubic yards.*
Hamburg	304.5	5,955,708	191,090	32.10
Nurnberg	111.8	2,020,815	40,348	19.64
Leipzig	.....	5,201,494	115,182	22.14
Cologne	185.8	3,010,653	66,624	22.12
Dusseldorf	37.9	729,560	49,704	68.18
Barmen	.....	1,550,761	13,472	8.68
Berlin	357	8,235,731	417,814	50.7
Sheffield	221	5,728,800	75,211	13.13
Average	.....	.....	.....	29.56

TABLE No. 6.—*Street sweepings removed, per unit of pavement, per year, American cities, 1913.*

	Length of streets.	Area of streets.	Street sweepings, per annum.	Street sweepings, per 1,000 square yards pavement, per annum.
	Miles.	*Sq. yards.*	*Cubic yards.*	*Cubic yards.*
New York (Manhattan, Brooklyn, Bronx)	1,433	28,481,042	859,539	30.20
Washington, D. C.	251	7,629,432	93,328	12.30
Newark, N. J.	238	5,060,980	123,322	24.30
Minneapolis, Minn.	96	2,610,687	60,900	23.30
Cincinnati, Ohio	608	9,959,328	128,030	12.80
Toronto, Ontario, Canada	521	7,260,186	237,678	32.70
Baltimore, Md.	571	6,585,138	268,328	40.80
Philadelphia, Pa.	1,071	17,059,545	395,000	23.10
Average	.....	.....	.....	24.93

TABLE No. 7.—*Monthly variation, in percentages, of garbage produced annually.*

	Cleveland.	Columbus.	Cincinnati.	Washington.	New York.	Detroit.	Chicago.	Borough of Richmond.
	Per cent.	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*
January	7.00	6.28	5.34	7.50	6.30	7.30	5.50	5.7
February	6.00	5.67	5.20	6.60	5.70	5.85	5.30	3.7
March	7.80	6.36	5.16	7.20	7.00	6.60	5.30	5.2
April	7.85	6.70	6.92	7.55	8.10	7.55	6.50	7.7
May	7.50	7.78	6.80	8.45	9.25	8.20	7.40	8.1
June	9.00	7.82	9.08	7.80	9.37	7.90	8.10	8.7
July	8.65	9.40	12.40	9.20	9.55	8.80	10.50	9.2
August	9.60	12.24	12.10	11.70	9.86	10.40	12.40	10.6
September	10.70	12.95	13.80	10.90	10.89	10.10	12.30	12.5
October	9.80	9.20	8.20	8.50	9.18	10.30	10.60	11.3
November	8.30	7.83	7.50	7.40	7.80	8.10	8.60	9.2
December	7.60	7.77	7.50	7.20	7.00	8.90	7.50	8.1

TABLE No. 8.—*Monthly variation, in percentages, of ashes and rubbish produced annually.*

	Cleveland, Ohio (State Board of Health).	Cincinnati, Ohio (State Board of Health).	Milwaukee (Hering).	Boston (Goodnough).	Borough of Richmond (Fetherston).
	Per cent.	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*
January	11.44	12.45	12.46	10.30	10.6
February	7.97	11.46	10.81	10.62	9.6
March	11.51	12.23	11.68	10.47	11.8
April	9.56	8.17	7.16	9.94	10.7
May	8.72	6.88	8.85	8.77	10.9
June	8.35	6.08	6.27	6.75	8.1
July	7.19	5.62	4.88	6.09	4.7
August	7.66	5.23	5.39	6.86	4.6
September	6.35	5.33	5.33	6.25	4.7
October	7.39	6.19	6.47	7.13	6.2
November	8.36	7.12	9.16	7.86	8.4
December	5.50	13.35	11.54	9.46	9.7

TABLE No. 9.—*Monthly variation, in percentages, of rubbish produced annually.*

	Buffalo.	Rochester.	Pittsburgh.	New York.
	Per cent.	*Per cent.*	*Per cent.*	*Per cent.*
January	8.62	8.50	8.27	6.43
February	6.43	7.58	5.83	6.28
March	7.78	8.05	7.92	7.54
April	9.79	8.78	9.44	8.26
May	11.97	8.90	10.92	8.31
June	10.38	8.00	9.63	8.63
July	7.69	9.35	8.26	8.94
August	7.24	8.67	7.84	9.54
September	7.30	7.99	7.57	9.68
October	8.95	8.94	9.48	9.80
November	6.54	7.49	8.33	8.77
December	7.31	7.75	6.49	7.82

One feature shown in Table No. 4, compared with the preceding table, is the separation of refuse into three classes as generally practiced in American cities, while in foreign municipalities as a rule all wastes are placed in one receptacle. Here, again, there is a clew as to the trend of practice regarding the collection and disposal of wastes. Foreign cities with small amounts of materials have practically standardized their methods and have adopted a combined collection and disposal of refuse, while American cities require the separation of refuse into three classes and disposal of each kind separately. Attention may be called to the variation in garbage production among the boroughs of New York City, as indicating the necessity for studying even subdivisions of a city for the purpose of determining the most suitable methods adapted to localities within the municipality.

It is not enough to provide general data as to the total volume or weight of refuse produced per unit of population or per year when considering the adoption of any method of refuse collection and disposal. The peaks and valleys of refuse production require determination. In American cities climate has the greatest influence in this regard, particularly in the production of garbage and ashes. Considering only American cities, Table No. 7, shows the monthly variations in the amount of garbage produced annually, and indicates generally an increase of approximately 50 per cent by volume during the summer season over normal production, with a slightly less percentage below the normal during the winter period. The same condition is approximately true among cities in the northern part of the United States for ashes and

rubbish collected together, as shown in Table No. 8. Rubbish separately collected has less seasonal variations on the whole than garbage or ashes, as indicated in Table No. 9.

These variations in the quantity of material produced at different periods of the year require careful consideration in the design of plant and equipment necessary for the economical operation of a collection and disposal system.

In addition to the amounts and seasonal variations of the various classes of waste, scientific methods of disposal depend upon the mechanical and chemical properties of the materials to be treated. Table No. 10 presents data relating to the mechanical analysis of mixed household refuse, composed of fine ash or material passing through a three-eighths inch mesh screen; coal and cinders, or unburned or partially burned coal; rubbish or generally combustible refuse; garbage (organic waste); and metals, glass, crockery, etc.

In foreign cities generally the amount of fine ash is greater than that shown in the analysis of mixed refuse in one of the boroughs of the city of New York, where tests were carried on for a number of years, and, surprising as it may seem, the amount of coal and cinders wasted is apparently less in New York City than in foreign cities, while the amount of rubbish produced is decidedly greater, except in Melbourne, Australia. It is interesting to note the relatively small proportion of garbage produced in German cities, and the larger amounts in Great Britain and New York. The variation in the metals, glass, and crockery discarded is hard to explain.

The system of refuse collection depends upon the method of disposal adopted. In foreign cities with few exceptions household refuse is collected in a mixed condition, while in the United States garbage is generally separated from other classes of waste, and disposed of either by incineration or by the so-called reduction method.

Where combined collections are in vogue great progress has been made in eliminating nuisances due to the escape of dust and odors while transferring refuse from the householders' cans to the wagon body. This is particularly true in the German cities, where a standard type of receptacle for holding wastes, having an attached cover, is so designed that it acts in conjunction with a loading device on the vehicle whereby the transfer is made without allowing the material to come into contact with the air or to be scattered about the neighborhood. In Great Britain and the United States not much progress has been made in collecting refuse so as to eliminate odors and dust, but there has been a widespread public demand for improvements of this character.

TABLE 10.—*Mechanical analyses of mixed household refuse.*

	Fine ash.	Coal and cinders.	Rubbish.	Garbage.	Metals, glass, crockery, etc.	Authority.
	Per cent.	*Per cent.*	*Per cent.*	*Per cent.*	*Per cent.*	
Berlin, Germany	45.73	25.77	5.18	20.0	3.32	Dr. Dörr.
Potsdam, Germany	60.98	18.61	2.28	8.26	10.87	Do.
Charlottenberg, Germany	36.58	37.00	5.08	4.85	14.49	Do.
Kiel, Germany	50.25	39.63	2.21	1.03	6.88	Do.
Frankfort, Germany	49.26	43.14	1.13	.58	5.89	Do.
Stoke Newington, England	(1)	42.92	15.4	34.43	7.35	Leask.
Kings Norton, England	(1)	45.4	9.3	39.50	5.2	Do.
Prahran, Australia	26.23	43.06	9.25	17.57	3.87	Calder.
Melbourne, Australia	42.81	26.55	11.57	14.31	4.76	Do.
Clifton, Borough of Richmond, N. Y.	31.1	19.5	10.80	31.10	7.5	Fetherston.
West New Brighton, Borough of Richmond, N. Y.	34.7	28.5	7.1	24.90	4.8	Do.

[1] Included in coal, cinder.

TABLE No. 11.—*Refuse disposal in the United States.*

Material and method of disposal.	Number of cities using this method.	Total population of cities using this method.
Garbage:		
Reduction	26	15,093,000
Incineration	41	3,618,500
Feeding pigs	11	1,266,000
Land fill	7	633,000
Dumping at sea	2	205,000
Rubbish:		
Incineration	33	4,178,000
Reclamation and fills	2	2,035,000
Land fills	5	672,000
Dumping at sea	2	720,000
Reclamation, fills, and incineration	1	4,600,000
Ashes:		
Land fills	11	8,092,000
Incineration	7	1,221,000
Dumping at sea	3	765,000
Street sweepings:		
Land fills	17	9,747,000
Fertilizer	3	645,000
Dumping at sea	4	1,506,000

Motor-driven collection vehicles have replaced horses in a number of foreign cities, and it is claimed that the cost of collection by this method is less than that by horse-drawn vehicles. In the United States, however, the horse, with cart or wagon covered or partly covered, still remain the standard types of apparatus for collecting refuse.

Practically every city uses some portions of refuse for land fills, and smaller cities use this method almost entirely until a point is reached where the cost of hauling to land fills exceeds the cost of disposal within the city limits, where the short haul offsets the increased cost of disposal by a scientific process. Table No. 11 summarizes the methods of refuse disposal practiced in cities having over 30,000 population in the United States. In cities of over 100,000 population a separate collection of garbage and reclamation of grease and tankage or fertilizer base is apparently the most popular practice, mainly from the standpoint of economy. Twenty-six cities, aggregating over 15,000,000 people, dispose of garbage by the reduction system, while 41 municipalities with about one-quarter the population incinerate the garbage. Feeding garbage to pigs, using it as land fills, or dumping it at sea is practiced in 20 of the larger cities in this country. Rubbish generally is either incinerated or placed on land fills. Ashes, in the majority of cities, are placed on land fills. Incineration of various classes of refuse, except street sweepings, is practiced generally among small cities and towns and is adaptable to all classes of waste, while reduction can only be applied to the treatment of garbage. Either system may be made sanitary in effect by proper design and efficient operation of the disposal works.

Garbage, when separated from other classes of waste and treated by the reduction process, provides two by-products: (1) Grease, varying from 3 to 8 per cent by weight of the original material, depending upon the location of the city and the character of the population. This grease is worth from 3 to 5 cents a pound and is used mainly for soap making. (2) Tankage or fibrous residue, after extracting grease and moisture, averages from 12 to 15 per cent by weight of the original material and contains fertilizing elements of value ($6 to $10 per ton) for various classes of crops. Net revenues from the treatment of garbage indicate the possibility of obtaining a profit at the plant varying from 75 cents to $1.50 per ton of garbage treated, depending upon the process used and the efficiency of the organization and management of the works.

Garbage-reduction works are generally located in sparsely settled sections, and as most of the plants are operated by private companies for commercial reasons, no greater attempt is made to eliminate odors than necessity demands. As a result, such plants have been frequent offenders on account of nuisances created,

though with proper design and management this drawback can be entirely eliminated or minimized to a point where the odors are not objectionable.

Probably the most sanitary method of refuse disposal is by incineration, as naturally all classes of waste contain some portions of combustible matter. Two methods of incineration are practiced in this country and abroad—(1) incineration of mixed household refuse, where all wastes are collected together and burned by the aid of forced draft at high temperature; (2) incineration of garbage alone or with portions of rubbish or ashes. By-products from high-temperature incinerators consist of steam power and clinker. Considerable information is available as to the heat values of the various classes of refuse, so that plants may be designed with some degree of knowledge concerning the proportions of the furnace required and the temperatures necessary to prevent the escape of noxious gases. The tables which follow summarize the available tests and the calorific values of various classes of household refuse in this country. For comparison with foreign cities, Table No. 17 is introduced. It is interesting to note in this latter table that the incineration of mixed refuse in German cities deals with a material high in ash, low in moisture, and generally lower in calorific value when compared with similar materials in New York City, though the conditions are reversed in San Francisco.

TABLE No. 12.—*Analyses of garbage.*

	Ether extract (grease).	Phosphoric acid.	Kjeldahl nitrogen.	Potash.	Authority and remarks.
	Per cent.	*Per cent.*	*Per cent.*	*Per ct.*	
Cincinnati, Ohio	4.02	0.29	0.64	0.28	Ohio State Board of Health report, 10 samples.
Cleveland, Ohio	3.85	.24	.64	.30	Ohio State Board of Health report, 28 samples.
Columbus, Ohio	3.96	.22	.59	.25	Ohio State Board of Health report, 31 samples.
Dayton, Ohio	3.83	.19	.51	.20	Ohio State Board of Health report, 30 samples.
Borough of Manhattan, N. Y.	6.79	.59	.94	.37	Lederle Laboratory, 4 samples.
Milwaukee, Wis	8.77	2.31	1.61	.....	R. E. W. Somers, 1 sample.
Borough of Manhattan, N. Y.	6.00	1.84	1.76	1.01	Otto H. Klein, 4 samples.

TABLE No. 13.—*Heat values of garbage.*

	Moisture.	Ash.	Combustible.	B. t. u. per pound.		Authority.
				Original sample.	Dry sample.	
	Per ct.	*Per ct.*	*Per cent.*			
Cincinnati, Ohio	76.7	3.66	19.70	2,000	8,553	Ohio State Board of Health report, 10 samples.
Cleveland, Ohio	75.6	3.20	21.16	2,057	8,459	Ohio State Board of Health report, 28 samples.
Columbus, Ohio	76.4	3.30	20.27	1,994	8,448	Ohio State Board of Health report, 31 samples.
Dayton, Ohio	80.6	2.57	16.82	1,712	8,776	Ohio State Board of Health report, 30 samples.
Canton, Ohio	74.4	2.72	22.88	2,304	.....	Ohio State Board of Health report, 4 samples.
Mansfield, Ohio	77.65	3.15	19.20	1,532	.....	Ohio State Board of Health report, 2 samples.
Marion, Ohio	73.5	2.95	18.60	1,925	.....	Do.
Steubenville, Ohio	75.0	3.59	20.91	2,100	.....	Do.
Zanesville, Ohio	82.3	2.47	15.23	1,413	.....	Ohio State Board of Health report, 3 samples.
Milwaukee, Wis	73.00	13.614	8.386	.....	4,522	R. E. W. Somers, 1 sample.
Borough of Richmond, N. Y.	73.26	5.14	21.60	2,233	8,351	B. F. Welton, 25 samples.
Toronto, Canada	47.66	26.35	25.99	2,572	4,914	Works Department Laboratory, 45 per cent rubbish, 4 samples.
Borough of Manhattan, N. Y.	67.0	4.49	28.51	.....	8,723	D. C. Johnson, 3 samples.
Do	71.4	3.72	24.88	2,597	.....	Klein, 1910, 4 samples.

TABLE No. 14.—*Heat values of street sweepings.*

	Moisture.	Ash.	Combustible.	B. t. u. per pound (original sample.)	Authority.
	Per ct.	*Per ct.*	*Per cent.*		
Cincinnati	43.9	42.20	13.9	1,445	Ohio State Board of Health report, 6 samples.
Cleveland	29.0	48.8	22.2	2,133	Ohio State Board of Health report, 2 samples.
Dayton	.....	82.1	17.9	1,690	Ohio State Board of Health report, 1 sample.
Borough of Manhattan, N. Y.	2.85	41.64	55.51	.....	New York Commission on Street Cleaning, 1907, 4 samples.
Do	27.45	35.69	36.86	3,665	Klein, 1910, 4 samples.
Borough of Richmond, N. Y., dry manure.	1.25	57.73	41.02	3,730	Lederle Laboratory, 1905, 2 samples.

TABLE No. 15.—*Heat values of rubbish.*

	Moisture.	Ash.	Combustible.	B. t. u. per pound.		Authority.
				Original sample.	Dry sample.	
	Per ct.	*Per ct.*	*Per cent.*			
Borough of Richmond, N. Y., West New Brighton.	5.78	13.87	80.35	6,832	7,251	B. F. Welton, 16 samples.
Toronto, Canada	33.02	7.82	59.16	5,449	8,135	Works Department Laboratory, Toronto, 2 samples.
Borough of Manhattan, N. Y.	11.50	7.59	80.91	6,701	7,572	D. C. Johnson, 4 samples.
Borough of Richmond, N. Y., Clifton.	6.3	11.5	82.2	6,636	7,082	A. E. Hill, 12 samples.

TABLE No. 16.—*Heat values of ashes and components of ashes.*

	Description.	Moisture.	Ash.	Combustible.	B. t. u. per pound.		Authority.
					Original sample.	Dry sample.	
		Per ct.	*Per ct.*	*Per ct.*			
Cincinnati	Ashes	7.8	61.70	30.5	3,087	3,348	Ohio State Board of Health report, 7 samples.
Cleveland	do	14.1	63.9	22.0	1,815	2,113	Ohio State Board of Health report, 6 samples.
Dayton	do	19.3	59.2	21.5	1,680	.....	Ohio State Board of Health report, 9 samples.
Chicago	Fine ash	1.92	77.75	20.33	3,167	.....	Bureau of Streets, Chicago, 20 samples.
Do	Cinders	1.16	53.0	45.84	6,941	.....	Do.
Borough of Richmond, West New Brighton.	Coal and cinders	1.34	39.93	58.73	8,396	8,510	B. F. Welton, 26 samples.
Do	Fine ash	1.20	77.40	21.40	2,846	2,880	B. F. Welton, 1 sample.
Borough of Manhattan.	Coal and cinders	7.65	31.82	60.53	9,310	.....	Otto H. Klein, 4 samples.
Borough of Richmond, Clifton.	do	2.8	23.3	73.9	10,946	11,260	A. E. Hill, 12 samples.
Do	Fine ash	1.9	72.6	25.5	3,119	3,180	Do.

TABLE No. 17.—*Heat values of mixed refuse.*

	Percentage composition of mixed household refuse.						Calorific value, moist sample, B. t. u., per pound.	Authority.
	Ash.	Moisture.	Combustible.					
			Carbon.	Hydrogen.	Cellulose, wood, etc.	Total combustible.		
Berlin	66.75	14.32	9.16	0.02	3.55	12.73	1,431	Dr. Dorr, Dr. Hampe, January, 1902.
Do	52.68	25.42	9.00	.06	8.10	17.16	1,636	Dr. Dorr, Dr. Hampe, February, 1902.
Potsdam	62.94	16.03	10.33	.42	4.78	15.53	1,877	Dr. Dorr, Dr. Hampe, November, 1903.
Charlottenburg	50.40	24.62	12.94	.02	7.04	20.00	2,115	Dr. Dorr, Dr. Hampe, January, 1902.
Kiel	63.96	10.12	18.86	.39	1.73	19.98	2,932	Dr. Dorr, Dr. Hampe, March 1903.
Wiesbaden	57.90	10.10	24.70	.32	3.72	28.74	3,982	Dr. Door, Dr. Hampe, March, 1902.
Dortmund	56.78	9.17	24.12	.77	3.40	28.29	4,021	Dr. Dorr, Dr. Hampe, July, 1902.
Frankfort	55.95	9.35	27.03	.30	1.18	28.51	4,033	Dr. Dorr, Dr. Hampe, December, 1902.
Karlsruhe	51.47	13.96	25.95	.43	3.24	29.62	4,044	Dr. Dorr, Dr. Hampe, November, 1902.
Wiesbaden	40.87	11.74	30.22	.41	3.24	33.87	4,672	Do.
Borough of Richmond, N. Y., Clifton.	35	30.1	.....	.....	.....	34.9	4,141	A. E. Hill.
Borough of Richmond, N. Y., West New Brighton.	46.08	19.74	.....	.....	.....	34.23	4,274	B. F. Welton.
San Francisco, Cal	27.2	49.9	.....	.....	.....	22.9	2,410	From specifications (Manson).

TABLE No. 18.—*Chemical composition of mixed household refuse.*

	Moisture.	Carbon.	Hydrogen.	Nitrogen.	Sulpher.	Oxygen.	Ash.	Remarks.
	Per ct.	*Per ct.*	*Per ct.*	*Per ct.*	*Per ct.*	*Per ct.*	*Per ct.*	
Clifton, N. Y., Borough of Richmond.	29.20	25.27	1.50	0.60	0.18	8.13	35.12	A. E. Hill, 12 samples.
West New Brighton, N. Y., Borough of Richmond.	19.74	26.46	1.30	.94	.....	5.52	46.04	Computed, Featherston.
San Francisco, Cal	49.9	13.90	1.70	.50	.....	6.8	27.20	Specifications, 4 samples (Manson).

TABLE No. 19.—*Cost of collection and disposal of household refuse.*

	Population.	Amount expended.	Per capita cost per annum.
Finsbury Borough, London	87,923	$49,028	$0.550
Sheffield	471,662	234,885	.498
Bradford	289,618	132,179	.456
London (old city)	364,061	123,675	.340
Manchester	731,677	414,548	.566
Paris	2,846,986	1,241,889	.435
Hamburg	976,000	286,613	.293

TABLE No. 20.—*Cost of collection and disposal of household refuse.*

	Population.	Amount expended.	Per capita cost per annum.	Authority and remarks.
Washington, D. C.	353,000	$158,550	$0.450	Year, 1913.
Newark, N. J.	395,000	190,605	.484	Do.
Cambridge, Mass.	110,000	65,000	.591	Do.
Chicago, Ill.	2,142,000	1,231,055	.574	Bureau of Census, year 1909.
Buffalo, N. Y.	415,000	272,075	.655	Do.
New Orleans, La.	334,500	169,635	.507	Do.
Louisville, Ky.	222,000	93,606	.421	Do.
Richmond, Va.	116,000	54,628	.470	Do.
Spokane, Wash.	99,000	59,036	.596	Do.
Galveston, Tex.	37,000	20,604	.557	Do.
Manchester, N. H.	69,000	22,534	.327	Do.
Salt Lake City, Utah.	87,330	39,416	.451	Do.
Harrisburg, Pa.	61,000	26,520	.434	Do.
Kansas City, Mo.	241,767	51,724	.214	Do.
Augusta, Ga.	41,000	14,968	.366	Do.

Further information concerning the chemical composition of mixed household refuse is provided in Table No. 18 for one borough in New York City, also San Francisco, Cal., where differences in the composition are again apparent, especially in the amount of moisture, carbon, and ash. It is evident from the statistics herein presented on incineration that the success of this method will depend to a large degree upon the preliminary investigations covering the heat values and chemical compositions of the waste in conjunction with the amount of material to be dealt with in any locality. Effective organization of the force employed and efficient management of the disposal works are essential in any type of plant in order to eliminate nuisances

The amount of street sweepings or cleanings removed from pavements in any municipality depends almost entirely upon local uses of the public thoroughfares. Only a general clue can be given as to the volume of street sweepings removed per unit of pavement per year. Statistics on this subject are not always satisfactory, but two tables have been compiled, one covering eight foreign cities, compared with eight American cities. Abroad about 29.6 cubic yards of material are removed per 1,000 square yards of pavement per year, while statistics for American cities show the removal of only 24.9 cubic yards. To one familiar with the use and abuse of streets in this country and in foreign cities, it would seem as if the figures should be reversed, and it is interesting to note that one of the cleanest cities in the world, Berlin, accounts for the greatest amount of material, 50.7 cubic yards removed per year from the unit of pavement area.

Two cost tables are presented on this subject, No. 19 covering the collection and disposal in seven foreign cities, and No. 20 containing similar information for 16 American cities. The average cost for the American cities is approximately 48 cents per capita per annum, as against 45 cents per capita per annum in foreign cities, where wages generally are less than half the standard rates in the United States. Apparently the refuse collectors in the United States are harder worked men than the foreign collectors.

The statistics herein presented summarize on a broad basis the best available data on the subject and are presented in concise form in the hope that those interested may find them of value.

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The CHAIRMAN. The papers to be presented at this session have been completed. It is especially desirable to have some formal debate on the subject, in view of the importance of the subject itself and the importance of the papers presented.

Dr. GUITERAS. As reference has been made by some of the gentlemen to the tropical cities and the request has been made directly that information be given with regard to what is being done there, I think it my duty to inform you on that point, although we are all devoting our time to learning all that we can about it.

In the last two years a system of separate disposal of sewage has been completed in Habana. The discharging place for this sewage of this large city could not be a more favorable one. The sewage of Habana is discharged by a separate system into the Gulf Stream. The same may be said with regard to the garbage and street and house refuse. Nothing could be more favorable than this. Still, undoubtedly, the management of this city refuse, the handling of it

in the city, the carrying of it to the lighters that go out to the sea to dump it into the Gulf Stream, is a disagreeable process at least, and perhaps accompanied with some danger. Therefore we have tried to introduce a system of incineration and we have had a large plant built for the purpose of doing away with the carrying out to sea. I must say that this plant, although it is completed, has not yet been used, because it is supposed to be expensive. I imagine that this means that the other system of dumping into the Gulf Stream is not so bad a one as was thought since we are not willing to go to a little more expense in putting into operation the already completed incineration plant. It may be true, as one of the gentlemen said, that these plants must be perfectly built and conducted. Probably our trials with the plant have shown that it was not properly built and that perhaps we were not very sure that we were going to handle it in a satisfactory manner.

As one of the gentlemen has said, when you have a system of sewage disposal in large cities you also have in the same city other systems. This means that we have still in Habana cesspools, especially the outlying districts. But certainly the introduction in the last three or four years of this enormous system of sewage disposal in the city of Habana ought to have made a striking difference in the amount of typhoid fever in the city. I am afraid it has not, and that has surprised me greatly. It is one of those subjects difficult to account for. Our typhoid-fever rate at Habana is rather high; not as high as in some American cities, but higher than in others. We do not believe that this is due to our water supply. The manner of distribution of typhoid and the character of the water are very strongly against the idea that it is a water-borne disease; but at any rate this very radical change in the disposal of sewage, the doing away with an enormous number of cesspools in the city of Habana, has not had any influence upon the number of cases of typhoid. In fact, typhoid has rather increased slightly in the last three years since this sewage system is in operation. We believe that our typhoid fever is a contact disease and that the distribution of it in the city of Habana is due to contact.

I was very much interested in the remarks that were made as to whether garbage disposal was a sanitary question. Of course it may become suddenly a sanitary question of intense importance, as it does, for instance, when plague appears in a city. Disposal of garbage may be considered almost one of the principal sanitary questions before a city. At a time of plague the disposal of garbage so that rats can not get at it and the utilization of that disposal as a means of doing away with rats by removing the food supplied to them are of the most extreme importance.

Of course I have been speaking of a large city, a rich city, as Habana is. When we come to the disposal of sewage and garbage in the rural districts, it is quite different. The human excreta are very commonly thrown upon the surface in the rural districts of Cuba, yet we do not have much hookworm there. Cuba is very far from presenting the same situation that Porto Rico does with regard to the number of cases of hookworm. It is not a national problem with us. The garbage, etc., of houses is usually disposed of by dumping.

Dr. AGRAMONTE. Perhaps I might be allowed to furnish a little additional information to Dr. Guiteras' remarks. This question of sewage and refuse disposal in Habana is in the hands of two different departments—the sanitary department and the department of public works. The department of public works has charge of the disposal of sewage refuse and garbage from houses, while the sanitary in a way supervises how this garbage is collected, etc. We have a national health organization, as you probably know. The head is the secretary of public health, a member of our cabinet. This national organization takes in every city and every municipality in the Republic of Cuba. Habana is only different from the other cities in having a special service in that direction. The question of public health can not be separated from the sanitary question in its engineering or medical aspects. We have sanitary ordinances which are applied to all the cities, all the municipalities in the island of Cuba, and they must all obey these ordinances. The ordinances refer to the disposal of garbage or its collection from houses, etc., providing the means under which the work shall be done, and, by the way, insist that it should always be collected in metal pails or barrels. The garbage is also indirectly under supervision of the sanitary department, while the street cleaning is in the hands of the department of public works in Habana. In the smaller cities of the island it is under the charge of the sanitary officers.

In Habana the care of the streets is divided into two parts. One is really the street cleaning and the other is the collection of manure from the streets. This is in the hands of private individuals, who utilize the manure for fertilizing purposes, and who also collect the manure from the large stables, public hack stables, etc., and sell it to tobacco planters in the eastern part of the island mainly. They collect it in large piles, ferment it, and then carry it into the interior. The manure from the private stables, of course, is carted off separately from the garbage and house refuse.

As I said, it is difficult to conceive how the medical question can be separated from the engineering or the question of sanitation. We have a particular condition in Cuba that is unlike, of course, the con-

dition in large countries. We have no inland waterways. Therefore the question of pollution of streams does not exist with us. The water employed for drinking purposes in large cities is not surface water, it is spring water; therefore the contamination of water supplies from streams and trains does not concern us. Trade wastes engage the attention of the sanitary department particularly lately with regard to the immense amount of waste produced in the distilleries of the large plantations, which throw their waste into the small streams, as we have no large rivers. But these small rivers have fish and the waste kills the fish, and sometimes a very unpleasant condition arises. This question is now being attended to. I believe Dr. Guiteras knows better than I do about this. The idea is to have these wastes go to a reservoir of some kind, remain there for a considerable period of time until they are self-purified, and then dumped into these rivers, when they would do less harm.

Dr. KEBLER. I was interested in some of the remarks made by Dr. Sedgwick, particularly that feature referring to the inhalation of street filth. Most of the material that is dropped on the streets or sidewalks is dried, and during a windy day is, of course, wafted into our faces, our nostrils, and our mouths. I have frequently wondered why we forbade spitting on the sidewalk and in a way invited spitting on the street. To my mind, there is not very much difference. As a matter of fact, the material dries as rapidly in the street as on the sidewalk. It is considered a matter of inconvenience, possibly, but I personally have never been able to see why such a distinct element has been made of that particular feature.

The CHAIRMAN. As there is apparently no further business, the chair will announce this session adjourned.

Adjourned at 11.26 o'clock.

GENERAL SESSION OF SECTION VIII.

NEW EBBITT HOTEL,
Tuesday afternoon, January 4, 1916.

Chairman, SAM. L. ROGERS.

The session was called to order at 2 o'clock by the chairman.

The CHAIRMAN. The program opens with a contribution by Dr. Edwin O. Jordan, department of hygiene and bacteriology, University of Chicago, Chicago, Ill., Dr. Jordan has requested Dr. Ransdell to kindly read his paper.

THE PURIFICATION OF WATER SUPPLIES.

By EDWIN O. JORDAN,
Chairman Department of Hygiene and Bacteriology, University of Chicago.

Discussion of water purification in this paper is limited to the hygienic aspects of the subject. Clarification of a muddy water, removal of an excess of iron, softening of a hard water are all ends desirable in themselves, but they are not purification in the sense in which that term is here considered. Removal of turbidity may be economically and esthetically important; installation of a municipal water-softening plant may be demanded by considerations of convenience and economy, but softening and clarification of water are never matters primarily concerning public health. If a community desires and can afford to pay for a clear or a soft water, it can get it. The degree of expense in this direction that is justified in comparison with other needs is a question to be determined by each community, bearing in mind that the demands of the modern city are many and urgent, and remembering that in but few instances are funds available to carry out all the measures of improvement that appeal to different groups.

Most citizens would agree in principle, if not in practice, that the sanitary purity or direct relation of a water supply to health is by far its most important feature. Consideration of purification of water may therefore be here consistently restricted to the methods of rendering a contaminated or potentially dangerous supply safe for use.

WHY PURIFICATION IS NECESSARY.

The present necessity for water purification in civilized countries is in the main a consequence of two factors: First, the greatly increased demand for water under modern conditions of life; second, the increasing density of population on most parts of the earth's surface. It is becoming more and more difficult to draw for a water supply of any size upon a body of surface water that is uncontaminated or at all events not liable to occasional or accidental pollution; as is well known infectious material discharged by a single human being is sufficient to poison many gallons of

water and to cause hundreds of cases of disease. It is difficult also to obtain the volume of water sufficient for a large and rapidly growing community. Many of the smaller towns and villages in the United States rely on deep wells as a source of supply, and from a sanitary point of view such waters are usually excellent. In many regions, however, the amount of available underground water is limited and if a large amount of water is required by a municipality, surface waters more or less exposed to pollution must be taken. Where surface waters are resorted to, the need for purifying them is so plain in some cases that there can be no question of its imperativeness, as with the Merrimack River used by the city of Lawrence, Mass.; the Hudson River, used by the city of Albany, and the Schuylkill River, drawn on by Philadelphia. In these cities simple inspection of the water source is sufficient to show that the river water used as a source of supply is contaminated with fresh sewage and in an untreated condition is grossly unfit for drinking purposes. Water purification in these cities has been followed by a marked diminution in the amount of certain diseases.

On the other hand, the need for purification of a surface water supply is not always so obviously urgent to the untrained judgment, and detailed observation of disease prevalence and of the bacterial character of a water is necessary before general agreement on the desirability of purification is reached. This has been the water supply history of some cities on the Great Lakes. The city of Cleveland hesitated for several years before undertaking the construction of a filter. Detroit and Buffalo have been rather recently convinced of the desirability of protecting their water supplies by chlorination.

Still other large cities are so fortunately situated in respect to surface water supplies that artificial purification for the time being is not considered necessary. These are practically all in localities where the water shed levied on is owned or controlled by the municipality, and where long storage of impounded waters in natural or artificial reservoirs can be trusted to effect a natural purification. New York and Boston are well-known examples of cities depending on protected and stored surface water.

THE DEVELOPMENT OF WATER PURIFICATION.

Public water supplies, although not uncommon in the early history of southern Europe, were practically unknown in the Middle Ages, and the large modern water supply systems have been developed for the most part in the last 70 years. Storage of water was undoubtedly practiced in antiquity, but was not consciously resorted to as a means of purification, and the first deliberate attempt at purification of water on a large scale seems to have been less than 100 years ago, when, in 1829, a slow sand filter was built by one of the London water companies. Even in this instance the immediate end in view was clarification of a muddy water, and it was not until the connection between drinking water and disease became manifest some 20 years later that the filtration of the whole London water supply was more definitely undertaken as a hygienic measure. Purification of public water supplies became general in England and on the Continent of Europe two or three decades earlier than in this country, owing perhaps to the greater density of population in many regions and to the glaring evidences of pollution in many streams serving as water sources. European cities that delayed or boggled water purification often suffered severely from water-borne diseases, as did the wealthy German city of Hamburg in the cholera epidemic of 1892–93.

In the United States, as in Europe, development of public waterworks has taken place almost wholly since 1850, and the introduction of methods of purification is yet more recent. A beginning in water purification had been made at Poughkeepsie, N. Y., and elsewhere before 1890, but progress has been much more rapid since that date, owing in large part to the impetus given to the study of water purification by the investigations of the State Board of Health of Massachusetts. These investigations,

begun in 1887, were soon followed by the construction of a modern sand filter plant at Lawrence, Mass. (1893), and the striking success of this filter in reducing typhoid fever served as an object lesson to the whole country.

It was calculated by Hazen that in 1900, 6.3 per cent of the urban population of the country (towns of over 2,500 population) were supplied with filtered water, while in 1911, according to G. A. Johnson, this proportion had arisen to over 20 per cent. The following table that I have compiled from the information given in the McGraw Waterworks Directory and from other sources of information shows the present condition in the larger cities of the United States.

TABLE I.—*Character of water supplies in cities of the United States with over 10,000 population in 1915.*

	Treated.		Untreated.		Unknown.	
	Number of cities.	Population.	Number of cities.	Population.	Number of cities.	Population.
Wells and springs	28	2,491,810	76	2,215,163	63	1,765,589
Rivers and streams	141	10,769,547	22	1,053,418	25	608,423
Impounding reservoirs	30	1,992,035	19	5,269,524	19	842,526
Lakes	38	5,408,206	25	1,866,312	16	464,690
Wells and rivers	15	571,566	5	92,301	7	452,812
Unknown					32	516,273
Total	252	21,318,164	147	10,516,718	162	4,645,283

It will be noted that while over 60 per cent of the total city population of the United States is at present supplied with water treated by some method of purification, the actual proportion of the population supplied with hygienically safe water is far greater. The water from deep wells and from storage reservoirs is unquestionably in large part of excellent quality, even if not subjected to artificial purification. It is fair to assume that 30,000,000 out of the 36,500,000 people living in cities with over 10,000 population are now provided with water initially pure or more or less effectively purified. Taking into consideration smaller towns and villages, it seems likely that at least 50 per cent of the total population of the United States is to-day supplied with water of a high degree of purity.

Hazen estimated that in 1904 water of a more or less unsatisfactory quality was supplied to approximately 52 per cent of the urban population of the United States in cities of more than 25,000 inhabitants; at present, 1915, this statement, as far as sanitary quality is concerned, would hardly hold true for more than 20 per cent.

MODERN METHODS OF PURIFICATION.

(*a*) *Storage.*—A high degree of natural purification of water can be effected by storage. When the water of small streams is impounded in a reservoir instead of being pumped directly into water mains important changes occur. Suspended matter in part sinks to the bottom and the water becomes clearer, the color of the water is usually lessened owing to bleaching by the sunlight, and the total number of bacteria in the water is materially diminished. Most important of all, any disease-producing bacteria that may have found their way into the tributary streams tend to perish during the sojourn of the water in the reservoir. A cardinal factor in bringing about the death of pathogenic bacteria in water is time. So far as is known, disease germs introduced into water never multiply under natural conditions, but progressively and rather rapidly die off. The longer a water can be stored, therefore, either in an artificial reservoir or in a natural lake or pond with protected shores, the less liable it is to harbor disease germs. This principle of storage, based on the high mortality of typhoid bacilli and allied bacteria suspended in water, is being utilised

apparently with high success in the treatment of many large surface water supplies. New York and Boston, as already mentioned, are relying mainly on this method to insure the purity of their supplies. The safety of the London supply is thought to depend very largely upon storage. Adequate storage is often all that is needed. In cities where other methods of purification are employed, preliminary storage is highly advantageous since it reduces the burden upon filters and in other ways facilitates the application of special purifying treatment.

(*b*) *Slow sand filters.*—The use of beds of sand carefully superimposed on gravel in water-tight basins and through which water flows by gravity was probably the first method employed for water purification (London, 1829) on a large scale. The earlier European filtration plants were all of this type. In this country slow sand filters have been installed at Albany, N. Y.; Pittsburgh, Pa.; Washington, D. C.; Philadelphia, and other cities. Through such filters water may be commonly passed at a rate of 3,000,000 gallons daily per acre of filtering surface, and if the water treated is not very turbid or badly polluted, a rate of 6,000,000 gallons or more daily may be permissible. It is important that the speed at which the water passes through the sand shall not vary suddenly or in different parts of the filter, and ingenious devices for regulating the flow are in use in order to maintain a uniform rate of filtration. Disturbance of the filtering surface by ice also impairs the efficiency of the operation and in some instances has been followed by outbreaks of disease.

One of the principal elements of expense in the operation of slow sand filters is the necessity for removing and eventually cleaning and replacing the thin upper layer of sand which becomes clogged in operation. The frequency with which the sand surface must be scraped and renewed depends largely upon the amount of suspended matter in the water treated and upon the rate of operation. The use of ample preliminary settling basins or storage reservoirs will lessen the operating cost, as well as introduce an element of safety. Taking into consideration the interest on the capital invested in construction and other proper capital charges, together with the cost of maintenance, the average cost of purifying water by slow sand filters is about $8 per 1,000,000 gallons under present conditions in this country. On the basis of a daily per capita water consumption of 125 gallons this involves an annual cost of about 36 cents per capita.

(*c*) *Rapid sand filtration.*—Slow sand filters are not adapted for use in many parts of the United States because the amount and fineness of the suspended matter in many American rivers leads to premature clogging of the sand and a total obstruction of operation. A somewhat different type of filter known as the mechanical or rapid filter has proved to have marked advantages in dealing with very muddy water, such as is found in the Ohio and Mississippi Rivers. If a turbid water is first treated with some coagulating chemical, such as sulphate of aluminum or sulphate of iron, it can be passed through sand at a much higher rate than is possible with the untreated water. The development of rapid filtration with the use of a coagulant has been largely a matter of American invention, and in its beginning depended to a great extent on the use of patented processes and mechanical devices protected by patent The expiration of some of these patents has opened the road for a wider application of this method and has been followed by important developments. Experiments at Louisville and Cincinnati have established the applicability of the coagulating process to large volumes of water, and at present rapid sand filters are in operation at Cincinnati, Ohio, Minneapolis, Minn., St. Louis, Mo., and many smaller cities. Suitable automatic devices for controlling the application of the coagulating chemical are indispensable, since any material excess or deficiency of the coagulant is fatal to successful or economical operation. Many of the earlier installations of rapid filters by private firms were not properly supervised, and in some cases the original plant was improperly constructed or allowed to deteriorate so that the whole process for a time fell into a measure of disrepute.

The cost of construction of rapid sand filters is much less than that of slow sand filters, but the cost of operation is greater. Reckoning all charges, the total cost per million gallons of water purified averages distinctly less (about $6 per million gallons) by the rapid than by the slow process.

(*d*) *Germicidal treatment.*—Although in the course of years a great variety of chemical substances have been proposed for the disinfection or partial sterilization of water supplies, only a few of these have won any extended practical application. The use of ozone for water sterilization possesses certain theoretical advantages. Several small plants using ozone have been operated in European countries, but in practice the relatively high expense of generating the ozone and bringing it in intimate contact with the water to be treated has so far proved an obstacle to the utilization of this mode of treatment for large supplies. It is possible that the availability of cheap electric power for generating ozone combined with other favorable factors may, under some conditions, render ozonization desirable. The development of cheaper germicidal processes, however, has checked, permanently perhaps, the general introduction of ozonization.

The objection of high cost obtains also with respect to the use of ultra-violet rays. These rays, which are conveniently generated by specially constructed lamps, have a high germicidal power, and quickly destroy bacteria in clear water. Experimentally ultra-violet sterilization has very desirable qualities, but thus far, owing to the expense of operation and to the necessity for a preliminary clarification of very turbid waters, it has not been used in this country for large scale installations.

The use of calcium hypochlorite, "chloride of lime," or "bleaching powder" has for some years past quite overshadowed other methods of germicidal treatment. Variations in the character of the water and in the composition of the commercial bleaching powder affect the amount that it is necessary to add to secure germicidal efficiency, but in general the quantity of the powder used ranges from about 5 to 15 pounds for each million gallons of water treated. The cost of bleaching powder under normal conditions has been less than 2 cents a pound; including the cost of application hypochlorite treatment costs not more than one-tenth as much as filtration. The action of the hypochlorite is similar to that of ozone and depends on the strongly oxidizing powers of the hypochlorous acid that is formed when the bleaching powder is added to water.

The advantages of the hypochlorite treatment are the cheapness, harmlessness, ease, and speed with which it may be employed. The chief objection is the liability to the production of disagreeable tastes or odors which its use entails. Chlorine gas itself has a distinctly unpleasant odor even in small quantities, and the action of the hypochlorite on certain organic matters present in water also generates disagreeable tastes and smells. Complaints on this score in communities where hypochlorite treatment of the water is practiced are especially common in cold weather. Waters differ in respect to their tendency to develop objectionable odors, and in practical operation some waters are very troublesome. An important improvement in the field of water disinfection has been the substitution of liquefied chlorine gas ("liquid chlorine") for calcium hypochlorite. The gas, which is generated by the electrolysis of brine, is dried, cooled, and compressed, and is then marketed in liquid form in portable cylinders under pressure. The advantages claimed for the use of the gas include superior economy and simplicity in regulation. Liability to cause unpleasant odors is said to be much less by this mode of treatment. Overdosing, however, may occur both with liquid chlorine and bleaching powder.

RESULTS OF WATER PURIFICATION.

When a polluted water that serves as a source of municipal supply is treated by slow sand filtration the most conspicuous immediate change in the health of the

community is a drop in the typhoid death rate. This has been demonstrated repeatedly in European cities, as in Hamburg, for example, and in many American cities. In Lawrence, Albany, Pittsburgh, and Philadelphia, slow sand filtration of a highly polluted river water has been followed by a reduction in the reported typhoid mortality to one-third or even one-fourth of that formerly prevailing. A decrease in water-caused infant mortality has also been noted.[1] It is yet unknown to what extent the connection between infant mortality and sewage polluted water supplies is due to infection with the typhoid bacillus. In some instances, though not in all, the so-called Mills-Reincke phenomenon has been observed, namely, a decline in the general death rate minus the typhoid component, and in the reported deaths from certain other diseases, such as tuberculosis and pneumonia, not commonly regarded as water borne.[2]

There is no doubt that some deaths from typhoid infection both in infants and adults have been and still are reported under some other designation. I have elsewhere [3] called attention to the decrease in reported deaths from "malaria" in Albany, N. Y., following the installation of a sand filter. It is unquestionably true that in other cities some of the deaths in the past reported as due to "malaria" or "typho-malaria" should have been properly classed with those from typhoid fever. Mistaken diagnosis may explain to some degree such decline in general death rates as can not be referred directly to the diminution in deaths specifically attributed to typhoid fever. Thus, in St. Louis, a correspondence can be noted in some years between the number of reported deaths from typhoid fever and the reported deaths from "malarial fever."

TABLE 2.—*Deaths reported in St. Louis.*

Year.	Typhoid fever.	Malarial fever.	Year.	Typhoid fever.	Malarial fever.
1890	140	226	1893	215	284
1891	165	216	1894	171	179
1892	441	336			

In more northern cities, where for various reasons the diagnosis of death from "malaria" is less likely to be made, the same correspondence can yet be noticed under certain conditions.

TABLE 3.—*Deaths reported in Chicago, 1891.*

Month.	Typhoid fever.	Malaria.	Month.	Typhoid fever.	Malaria.
January	67	7	April	136	18
February	61	9	May	408	22
March	71	16	June	167	7

There seems no escape from the conclusion that at least some—probably a large proportion—of the deaths recorded as due to "malarial fever" in these cities were in reality caused by typhoid infection.

It has further been shown by Dublin [4] from a study of insurance records that the normal expected mortality is doubled among typhoid convalescents during the first two years after their recovery from the disease. In his statistics tuberculosis, diseases of the heart and kidneys, and pneumonia were prominent among the causes of death in a limited number of typhoid patients subsequent to recovery. If this

[1] McLaughlin, Reprint from Public Health Reports, No. 77, 1912, Washington, D. C.
[2] Sedgwick and MacNutt, Jour. Infect. Dis., 1910, 7, p. 489.
[3] Transactions, Amer. Soc. of Civil Engineers, Inter. Eng. Congress, 1905, 54, D, p. 206.
[4] Amer. Jour. of Pub. Health, 1915, N. S. 5, p. 20.

conclusion proves generally valid, there must always be expected some lessening of the general mortality in addition to that due to the typhoid component, and perhaps in some cases a measurable diminution in the death rate from tuberculosis and other diseases accompanying a decrease in typhoid fever due to water purification. In a word, certain individuals appear to be so affected by the typhoid infection that, although surviving for a time, they die within two years from tuberculosis or cardiac lesions. To what extent the Mills-Reincke phenomenon and Hazen's theorem are explicable on this basis is a matter for further investigation to determine.

Granting that many deaths from typhoid fever and its sequelae are prevented by slow sand filtration, the question may be raised as to what degree of safety is attained by this method, whether absolute or limited. The necessity of care in operation is well known. Bacterial and other observations clearly show that dangerous bacteria may pass through the sand, if there is any "accident" to the filter or any "disturbance" of its normal action. The epidemics of cholera at Altona, Germany, and typhoid fever at Lawrence, Mass., illustrate the way in which the formation of ice can interfere with the safe operation of a filter.

While the harm from such unusual interruption of normal filter action is sufficiently demonstrated, it is not so easy to measure the degree of danger existing under more ordinary conditions. Reliance on bacterial averages of effluents may be misplaced, since a low average may be reached even if occasional breaks occur in a long series of low numbers. Should typhoid bacilli pass through a filter during one hour in 24, or for one day in the year, absolute protection is plainly not afforded. While the data for a final judgment on this point do not exist, it must be admitted that there is some evidence that the attempts to treat a highly polluted raw water, place at times too great a burden on the filter. Intestinal bacteria of the *B. coli* type may appear in the effluent in such cases in numbers thought by some observers to indicate danger.[1]

Among the recent attempts to establish standards for safe drinking water may be noted the report of the commission appointed by the United States Treasury Department to consider standards for water supplied to the public by common carriers engaged in interstate commerce.[2] The commission reported as follows: "(1) The total number of bacteria developing on standard agar plates, incubated 24 hours at 37° C., shall not exceed 100 per cubic centimeter; (2) not more than one out of five 10 cubic centimeter portions of any sample examined shall show the presence of organisms of the *B. coli* group." A study of the records of filtration plants shows that in some instances the application of such a standard would lead at times to the condemnation of filter effluents. It has been suggested that the standard proposed is too severe for general municipal water supplies,[3] and perhaps this is a just criticism, but in any case it is clear that the margin of safety in some filtration plants is not very great.

The results of rapid or mechanical filtration are essentially similar to those of slow sand filtration. The percentage bacterial removal reaches practically the same height as in the slow sand filter, and a marked decline in typhoid fever has been observed in many cities following the introduction of rapid filters. In Cincinnati, Ohio, Columbus, Ohio, Paterson, N. J., and other cities, the typhoid death rate has sunk to low figures after rapid filters were installed. The necessity for careful and unremitting supervision of operation is quite as great in the case of rapid filters as with the slow sand type. The safety of the mechanical filter effluent is no more certain or absolute than that of slow sand filters.

Excellent results as regards bacterial efficiency and security from typhoid infection are achieved by bleaching powder and by liquid chlorin treatment. The chief

[1] McLaughlin: Reprint, Public Health Reports, No. 204, Jan. 26, 1914.
[2] Bacteriological Standard for Drinking Water, Reprint, 232, U. S. Public Health Reports, 1914.
[3] Fuller: Jour. Franklin Institute, July, 1915, p. 42.

difficulty experienced in this mode of water purification lies in the close approximation for many waters of the limit of germicidal efficiency and the limit of inoffensiveness. If unpleasant odors are produced by the chemical, the maintenance of an adequate bactericidal strength often proves difficult in the face of complaints from hundreds of water consumers. The city of Cleveland is thought to have suffered excessively from typhoid in 1913 in consequence of a decrease in the dosage of hypochlorite.[1] Temporary cessation of the hypochlorite or reduction to an amount inadequately germicidal may sometimes be followed by a definite typhoid epidemic, as in the outbreak investigated by the writer at Quincy, Ill., in 1913.[2]

A remarkable reduction of typhoid has been observed in some cases to accompany the hypochlorite treatment. The experience of Milwaukee is in point.

TABLE 4.—*Deaths from typhoid per 100,000 population, Milwaukee, Wis.*[3]

1906–1910 (average)	27
1911 (hypochlorite used intermittently)	19
1912 (hypochlorite used continuously after September, 1912)	25
1913 (hypochlorite used continuously after September, 1912)	11
1914 (hypochlorite used continuously after September, 1912)	8
1915 (estimated, liquid chlorin treatment begun Mar. 31, 1915)	5

Other similar instances are on record in which a marked typhoid decrease has been chiefly attributable to chlorin treatment of the public water supply. In such cases it is interesting to note that although clarification is not effected by the chlorin treatment, the sanitary success seems at least as great as when filtration is practiced.

One noteworthy development of the chlorin treatment has been its application either to the raw water or to the effluents of slow sand and rapid filters. Hypochlorite dosage of the water applied to filters or of the filter effluents has in fact become an almost universal procedure. (See Table 5.) It does not yet appear that this practice is accompanied by any measurable decline in typhoid fever in cities previously served by a modern well-operated filter.

TABLE 5.—*Methods of water purification in cities of the United States with over 10,000 population.*

	Slow sand filtration.		Rapid sand filtration.		Chlorin treatment alone.
	With chlorin.	Without chlorin.	With chlorin.	Without chlorin.	
Number of cities	13	19	105	46	57
Population	2,886,233	1,073,290	7,343,987	3,835,980	5,793,419

THE OUTLOOK.

A few probable developments in water purification in the United States can be forecast. It seems likely that the public demand for a clear, as well as a purified water will increase and that sand filtration of the mechanical type will become more general. It is also probable that the increase in pollution of surface waters consequent upon growing density of population will tend to overburden filter plants and that if the raw water can not be protected, chlorination will be resorted to as an adjunct to filtration. In the near future practically all surface waters not adequately purified by protected storage will be treated by some purifying process. Already approximately 80 per cent of the population of cities of over 10,000 inhabitants and over 50

[1] Collins and Perkins, Cleveland Med. Jour., 1914, 13, p. 786.
[2] Jour. Infect. Dis., 1913, 13, p. 16.
[3] From information kindly furnished me by Dr. G. C. Ruhland, health commissioner, Milwaukee.

per cent of the total population of the country are supplied with purified surface water or from ground water sources for the most part of excellent sanitary quality. At the present rate of progress water-borne disease in the cities and larger towns of this country [1] will within 10 years be relatively rare.

The CHAIRMAN. If I am not mistaken it is the rule in this section to grant a limited time to the discussion of any paper under consideration.

Col. HOFF. I move that the discussion be postponed until after the reading of other papers of a similar character.

Seconded and approved.

The CHAIRMAN. The next contribution is by Prof. E. M. Chamot, of the laboratory of sanitary chemistry, Cornell University, Ithaca, N. Y. I think the secretary has had a communication within the last few minutes from Dr. Chamot.

Secretary WHITMORE. This letter is from Ithaca, N. Y., dated January 4, 1916:

An attack of rheumatism and neuritis will prevent my attendance at the congress, and therefore the reading of my paper on Tuesday afternoon. E. M. CHAMOT.

The CHAIRMAN. We are sorry that the doctor is not present. His paper will go into the proceedings if there is no objection. Hearing none, it is so ordered.

THE APPLICABILITY OF MICROSCOPIC METHODS TO THE STUDY OF WATER-SUPPLY PROBLEMS.

By E. M. CHAMOT,

Professor of Chemical Microscopy and Sanitary Chemistry, Cornell University.

The great desideratum in all investigations involving the quality of a water supply or the efficacy of a system of water purification is that the results of the tests or analyses shall be available in the shortest possible time. It is therefore no exaggeration to say that the most serious problem which confronts the water analyst and water works official is that of obtaining information concerning the quality of a water in question before such water can have reached the service pipes and have been used by the consumer. That our present methods are in the great majority of cases too slow and hence inadequate will be gainsaid by but few analysts and sanitarians, for year by year the increasing number of water purification plants of the rapid American type which are seldom properly operated forces upon our attention the fact that in the majority of these plants the true quality of the filter effluents can not be known until some hours after the water has been drunk by the public, since in most of these plants the rates of filtration are very high and the capacity of clear wells or distributing reservoirs relatively small.

Granting that it is intelligent supervision of the plant and not analytical control which is of the greatest value and all important, we are forced to recognize that the knowledge gained by the analyses must be regarded as documentary evidence available for reference and study, to guide in the future operation of the plant, and to serve as proof, in the event of controversy, of the quality of the water at the time the sample was taken.

[1] Jour. Amer. Med. Assoc., 1915, 64, p. 1322.

Since it is essential in all bacteriological methods that time be allowed for the growth and development of bacterial colonies it is unlikely that any culture medium can be discovered containing materials which will so stimulate and accelerate growth as to materially reduce the time which must now elapse before we are able to obtain the results we need in order to pass intelligently upon the waters in question. But if we are willing to recognize the quite obvious fact that essentially that which we are striving for is always in reality an opinion as to quality and not very accurate numerical results, then we may hope to add to the present accepted standard methods, supplementary tests yielding approximate results, easily and very rapidly obtainable. The development of such methods will enable the analyst to make many examinations of filter effluents in the course of a day. On the other hand very frequent platings of effluents from a number of filter beds is a task requiring too much time, labor and expense to be generally practicable. Few water purification plants indeed are financially able to perform the number of daily examinations of water that good management and ordinary common sense require. It follows, therefore, that there is but one system of very rapid bacterial enumeration which we may hope to successfully develop and this is a direct count by means of the microscope of the bacteria present. Although a number of such direct microscope count methods have already been proposed they have attracted little attention and have never received the study and trial as applied to routine work which they deserve and to which they are entitled. Most of these direct microscope count methods are modifications of the Hesse suggestion or that of Müller. In the Hesse [1] method the bacteria are concentrated by filtration through a bacteria proof filter, while in the Müller [2] method separation of the bacteria is accomplished by the centrifuge. A portion of the concentrate corresponding to a known volume of the original sample is then spread upon an object slide, fixed, stained, and examined. By means of a coordinate rule eyepiece micrometer adjusted to cover a known area of the preparation the stained bacteria are counted and from these counts the total number of bacteria per cubic centimeter can be calculated.

These methods are capable of yielding results bearing a very fair approximation to the colony counts obtained on gelatine. The numerical figures are usually a little lower than the standard count, being from 90 to 98 per cent of the latter. It is not my intention to here discuss the details of these microscopic methods nor to burden you with a recital of modifications and improvements. It is my wish to point out that methods exist which will enable us to obtain an idea as to the number of bacteria present, with little labor and expense and a total expenditure of time of not over an hour. In actual practice, after a little familiarity with the technique, we may obtain a count of the bacteria present in from 30 to 45 minutes, corresponding to 94 to 95 per cent of the counts we will obtain on gelatine at the end of 48 hours.

We have here, therefore, even granting its inaccuracies, a means at our command of very rapidly estimating the number of bacteria present in a sample of water with little labor and no disagreeable after-cleaning of dishes and apparatus and no appreciable waste of material. We can also by means of microscopic methods, make very frequent tests of filter effluents in rapid American system plants and obtain an idea of what the filters are doing, and this before the water can have reached consumers, a matter of prime importance when dealing with questionable efficiencies due to so-called air-bound filters, filters overtaxed to take care of some sudden emergency, filters whose normal run has been greatly shortened through clogging by the sudden development of some organism, or filters in which the upper or effective part of the filter bed has ruptured through sudden changes of head and loss-of-head. All of these conditions are apt to arise in any and every plant. The quality of the filter effluents is then immediately in question. If the number of bacteria in an effluent rapidly increases and the raw water is a contaminated one, it is only a matter of a short

[1] Hesse. Ztschr. f. Hyg. u. Infekt.-Krankh., 69, 522; 70, 310.
[2] Müller, Arch. f. Hyg., 75, 189; 82, 57.

time before this effluent will contain objectionable species of bacteria. It is rare indeed that organisms of the *B. coli* group are present in numbers in a raw water of low count and still rarer in filter effluents from properly washed and operated filters, unless these effluents run relatively high in bacteria. To this rule, however, there are exceptions. One interesting and very unusual case of this sort has come under the speaker's personal experience. A new unstripped reservoir, formerly employed as pasture land, was flooded in the spring, then followed a serious drought during the summer months. During the latter part of the summer the water in the reservoir became very low and stagnant. The counts on gelatine at 20° and on agar at 38° became substantially identical, averaging 200 colonies per cc. with practically every colony one of the *B. coli* group. Filter effients gave from 10 to 30 colonies per cc. on gelatine at 20° at the end of 48 hours, yet with this low count it appeared that from 10 to 20 of these were to be ascribed to the *B. coli* group. A direct microscopic count in such a case would give information of little value.

No doubt many other less striking unusual cases could be cited, yet they are unusual, and it will be found that in the vast majority of days in the year where questions involving the doubtful efficiencies of filters arise, direct microscopic counts will yield all the information necessary for the guidance of the plant superintendent. Were such methods studied, developed, and adopted in practice, the public would be insured a water of a much better quality. It seems to me, therefore, that we can not afford to longer ignore the practicability of such control methods.

There is also another valuable application of the method of direct microscopic bacterial count which is worthy of note and trial. A daily problem of the water analyst is that of deciding upon the dilution of a given water under examination which will yield him plates with not over 200 colonies developing per cubic centimeter at the end of 48 hours. If he is in doubt, several dilutions must be made, involving a loss of time, labor, and culture media. A direct microscopic count gives information with little loss of time and labor which may be utilized to good advantage in subsequent plating, while at the same time an excellent idea of the bacterial quality of the water is also obtained.

The one most serious drawback to direct microscopic counts undoubtedly lies in the little evidence diagnostic of species which it affords. We need in all cases not only an enumeration of the bacteria present but also information as to their species or groups. It may be possible that the method can in the near future be improved so as to afford at least a slight diagnostic value over and above the information yielded by the morphology of the organisms seen, but it is doubtful whether this phase can be developed to any satisfactory degree. In spite of these drawbacks, the water analyst should be willing to recognize the fact that direct microscopic counts are invaluable in the majority of everyday water problems.

There is only one type of water where such an examination is obviously of no value and this is in the analysis of "sterilized" or "disinfected" waters. Here we meet with the question of not how many bacteria are present in the water, but how many are living. Direct microscopic counts give us only the bacteria present—living or dead cells are alike counted. Plating methods give us only the count of those living and developing at the end of a given period of incubation. Both methods together carried over a long period of time should yield data of inestimable value. Nor is it beyond the range of possibility that staining methods are discoverable which will differentiate between living and dead cells.

The term "microscopic examination of water" has become through usage so closely associated with biologic, limonologic, or planktonic studies that its broader field of usefulness and sanitary applications have been almost lost sight of and generally neglected in America, and our standard methods for the examination of water fail to contain a single statement or suggestion as to the microscopic examinations, save for searching for odor and taste-producing organisms.

The study of water sediments, of suspended matters, the association of certain species observed in large numbers with that of a suitable environment necessary for their development, which environment is of an insanitary character; the presence of forms of life in a water which should be absent and could not possibly exist were that particular source free from pollution, are matters which no modern water analyst can afford to ignore. Many times a microscopic examination will solve a difficult problem. Permit me by way of illustration to briefly cite several cases of the kind of application we may make of microscopic sediment examination.

A small stream flowing through the grounds of a large corporation developed during the summer months a foul odor. In order to abate the nuisance it became necessary to find the cause of the trouble. A number of drains from laboratories, shops, and houses discharged into the stream. Chemical and bacteriological analyses eliminated one by one these drain lines as the direct cause of the nuisance. Samples of the water of the stream taken above these drains gave on chemical analysis evidence of gross pollution, while the bacteriological examination showed the presence of fecal and intestinal organisms. The analyst held that the water was receiving sewage. This was denied upon the basis that the sediment in the stream was not of the character and color met with in small brooks which are sewage polluted to an extent of giving off foul odors, and moreover the presence of fecal and intestinal organisms was to be expected, since a large stock farm was located upon the drainage area of the stream less than a mile above the point of sampling. It should be explained here that the brook flowed through a relatively long line of tile under a roadway sidewalk and filled-in ground and the samples were taken at the lower end of this culvert. The water analyst insisted, however, that the cause was sewage and that search should be made for a broken sewer line or an overflowing cesspool. Another factor entered in the problem in that the stream water varied greatly in character at different times of day, seeming to indicate an intermittent sewage discharge. The matter rested here through the winter and spring, but the next summer the odor became unbearably foul. Analyses showed a greater amount of contamination than before and again of marked variation in amount. Microscopic examination was resorted to with most excellent results. It was possible to demonstrate that the stream carried at times relatively large amounts of wood pulp and that this wood pulp was of the character of that of the toilet paper employed in the water-closets of the corporation, and further that the appearance of this disintegrated tissue paper coincided with the periods of maximum odors. This was evidence of a character not to be ignored. The sewer line was traced, found to cross the culvert tile above referred to, and excavated. The culvert tile were found to be cracked, the sewer tile above sunken on each side where it crossed the stream tile, opening up the sewer-tile hubs. Fine material was percolating through the loose soil and entering the little stream.

Here we have a very striking example of the value of microscopic examination in aiding in locating the exact cause of the nuisance in a water known to be grossly polluted and further of pointing out the remedies which should be applied to abate a nuisance. As a matter of fact, the microscopic examination alone gave all the information necessary, and had it been applied in the first summer it would have solved the problem without recourse to either chemical or bacteriological analyses.

Similarly in the case of drinking water, ofttimes both chemical and bacteriological examinations prove a water to be unfit for household use, yet the cause of the trouble is obscure or indeterminate. In the majority of such cases the microscope will usually supply the missing links in the chain of evidence. An excellent example is afforded in a problem arising in the case of a drilled well. The facts were these: Two old people died under circumstances pointing to the water of their well as the cause. The small farm was purchased by a city contractor and the house and its surroundings cleaned and repaired. The well, 95 feet deep, drilled in the rock and cased for some 60 feet, received special attention. A huge slab of concrete, 10 feet square and 2 feet

thick was cast about the well casing, a small catch basin with tile drain for leading off the water was provided to prevent water pumped from the well from flowing upon the soil in the vicinity of the well casing and seeping back into the well. Having thus improved the property and protected the well, two years later the new proprietor requested an analysis of the water. This analysis need not be given in detail; both chemically and bacteriologically the water was bad and the microscopic examination of the sediment pumped from the well disclosed a remarkable state of affairs, in that fragments of all sorts of ordinary articles of food and household débris could readily be detected and identified. These included cereal and potato starches, cooked and raw; muscle fibers; fragments of human hair and those of domestic animals, cotton, wool, and linen fibers dyed and undyed, such as would be found in the sweepings from carpets and floors; in other words, all the material normally to be found in dishwaters and laundry and household wastes.

It was obvious that dishwaters and slops had penetrated into the well, but no evidence as to just how this had taken place was obtainable for some time. The cesspool into which dish and laundry waters were being discharged was water-tight and so situated as to preclude any possibility of this source of contamination. The nearest neighboring farmhouse was over 3 miles away. Floor sweepings were being burned. The surface of the ground round about the well and the house afforded no possibilities of surface waters entering the well. There existed no visible drains. It was therefore surmised that the pollution must date back to the time before the improvements were made and that there must have been some drain line from the kitchen sink past the well. Upon investigation this supposition was found to be correct. There formerly did exist a subsoil wooden trough passing close by the well, but the manner in which the water of the well became befouled was not that anticipated, namely, a break in the trough and a leaky well casing, but proved to be due to a joint in the shale rock forming the precipitous bluff of a lake. The abandoned drain discharged over the edge of this bluff about 122 feet high. The dirty water struck a ledge upon the rocky wall some 70 feet down from the top. This ledge was formed at a joint in the strata and the inclination of the strata was such (so far as could be observed) as to allow a percolation of water to a level just below that of the water table of the well. By digging into the joint a short distance material was found of the same sort as that forming the sediment in the well water. Inasmuch as two years had elapsed since the wastewater drain had been abandoned and the well had been pumped dry on many occasions, it was evident that the polluting material had completely filled the joint and would render the well water unsafe for an indefinite period. The more the well was pumped the more the putrefying material could enter.

It is further worthy of comment that the water of this well was long regarded as a sulphur water because of its hydrogen sulphide odor. The milky turbidity was believed to be precipitated sulphur. The water being very cold, and high in dissolved gases, it was much sought after in the neighborhood as a mineral water, and its powerful cathartic effect was ascribed to purgative salts in solution. This is one of the only moderately deep-seated waters, cold and with an odor of hydrogen sulphide which the speaker has yet met with where the sulphureted water derived its odor and taste from putrefying material.

This case has been gone into at length because it is an exceptionally good example of the value of microscopic examination of sediments. It is to be especially noted that the microscopic examination not only solved the problem of the exact nature of the polluting material but eventually led to the discovery of its source and demonstrated that the well water must be indefinitely abandoned. We must not forget that a properly conducted water examination should give answers to three questions: (1) Is the water fit for household use; (2) if unfit,what is the trouble?;(3) how can it be permanently improved? To these three a fourth sometimes arises: Will the water probably continue to remain good or bad?

In the same class but of a different type fall those cases of microscopic examination of sediments and suspended matters disclosing finely divided wood pulp from chain pumps having wooden pump tubes, or an emulsion of oily droplets, etc., from pumps lubricated with an excess of oils and greases. Such waters yield high oxygen consumed and high loss-on-ignition, with the total solid residues usually blackening on ignition but all other chemically determined constituents low and usually low bacteria. The microscopic examination here serves to elucidate the cause of these high results and renders the interpretation of the entire analysis simple and certain. Without the microscopic examination the analyst is apt to be sorely puzzled.

Time forbids giving other examples although a large number might be cited. Yet it is remarkable how seldom the water analyst has recourse to this most valuable aid to assist him in forming an opinion as to the character of a water in question and as to the means for improving its quality.

The examination of sediment and suspended matters in waters for the possible presence of animal parasites is also too often neglected as a matter of routine work; in at least two instances the speaker has found the ova of the common tapeworm in spring waters submitted to him for analysis. It is true that these are but two instances in some twenty-odd years of experience as a water analyst, yet similar examples are apt to arise at any time, and if we are to really serve our clients, we must be prepared to adopt every and all means at our disposal.

That branch of microscopic examination devoted to the detection of the specific cause of bad odors and tastes in impounded waters is too well known and too generally employed and the necessity for its practice too firmly established to necessitate any consideration by me; but the study of the plankton causing rapid clogging of filters in rapid American systems is receiving altogether too little attention by analysts in charge of filter installations. It is not uncommon to have the period of service between filter washings cut down fully 95 per cent in the course of two or three days, due to the sudden multiplication of organisms of one species or another, thus forcing the purification plant to its capacity and not infrequently rendering its operation almost impossible. A knowledge of the species causing the clogging is imperative in order that the trouble may be intelligently fought. Even less attention is being paid to the influence of certain organisms in loosening the sand beds or at least in some way lowering efficiencies. There seem to be good reasons for believing that some of the lowering of efficiencies due to the pocketing of air within the filter beds may be due directly or indirectly to the action of organisms—directly when the organism effects a liberation of gases in the water, indirectly when through their action in forcing sand grains away from one another they form a space where air eventually accumulates. If there are a large number of such pockets formed, the available filter area may be greatly reduced and the filter finally taxed beyond its capacity, its loss-of-head rapidly increased, and finally the pocketed air rising loosens the bed and we have an airbound filter bed. Actually in practice, however, we frequently encounter what amounts substantially to airbound filters without the air rising as in typical cases, for the air clings tenaciously to certain sand grains which are coated with a film of such a nature as to hold the air. In such an event the filter may not "break," but its bacterial efficiency falls.

In our purification plants we have paid considerable attention to the effective size of the sand and its coefficient of uniformity, but we have absolutely ignored the question of the adsorptive powers of sands of different sorts for the coagulants we are to employ in the specific waters to be treated. Usually a newly constructed filter bed does not yield as high an efficiency as after it has been in use for a longer or shorter period, or until it has become "seasoned" or "ripened," as it is sometimes stated. It is the commonly accepted theory that the bed becomes efficient as soon as the sand grains acquire a thin coating of coagulant or a thin film of protoplasmlike material. This surrounding envelope is held by such grains of sand by virtue of their adsorptive

power for the particular kind of colloidal matter present, and it is probably largely by reason of the adsorptive power of the colloidal matter for the materials which we wish to remove that we obtain the efficient filtration we meet with in practice. It seems reasonable in the light of the recent developments of colloidal chemistry to regard the mechanical sand analysis expressed in terms of effective size and uniformity coefficient as giving us information only of the rates of flow we may expect through beds of the unclogged (uncoated) sand bed, but the purification efficiency of the bed must be measured largely by the adsorptive power of the sand for the colloidal matter and its ability to retain this adsorptive property. If we take sand from seasoned filter beds and examine it wet under the microscope just as it is, or treated with an aniline dye (congo red or benzo orange for basic aluminum sulphate treated waters), we will find a relatively large number of sand grains with no colloidal coating whatever, or with colloidal patches instead of coatings, and we will further find that the relative proportion of coated and uncoated grains is quite different in sands of different sorts. We need, therefore, to investigate sands with respect to their adsorptive powers. There is little question that the differences in efficiencies of different filter plants is a matter largely of adsorption of colloids and the power of the sand grains to tenaciously hold these adsorbed colloids in waters containing substance which through their chemical action might cause the colloidal envelopes to loosen and disintegrate.

It is safe to conclude that the sanitary engineer in writing his specifications for sand beds ought to be able to include details looking toward the use of a filter material of high adsorptive power. Were he in possession of this knowledge, much progress could be made, and in the opinion of the speaker we would meet with fewer plants of doubtful efficiencies.

Much interesting information as to the actual condition of the sand in the filter is to be gained by periodic microscopic examination of sand before and after washing a filter and studying the sand just as it comes from the beds, staining it to render the film more easily recognized, and also through examinations of sand after treating it with dilute hydrochloric acid. In many waters it will be found that in addition to the colloidal coating a film or a conglomerate of fine crystals of calcium carbonate coats the sand grains, and this when no lime or soda ash has been applied to the water. It is not clear whether this lime coating is beneficial or objectionable, whether it tends to cause colloids to deposit or prevents their adsorption. A fertile and highly interesting field upon which considerable work should be done is here open to the investigator. In one filter plant with which the speaker is familiar this tendency of calcium carbonate to deposit upon sand and gravel has been at times so great as to rapidly lead to the formations of patches of conglomerate in the bed, rendering washing of the filters inefficient and certain areas of the beds impermeable.

Occasionally the chemist finds it important to ascertain the nature of the salts deposited during evaporation or heating. The usual method consists in performing a quantitative analysis of the solid residue and then computing the so-called hypothetical combinations.

Few analysts appear to be aware of the fact that a microscopic study of the properly obtained solid residue will in most cases not only enable him to identify most of the salts which have separated but also to form a very good idea of their relative proportions with a certainty that is as surprising as it is simple and rapid.

There is absolutely no question whatever that microscopic qualitative analysis methods are the simplest, most rapid, and most certain that are at present available for the detection in water of minute quantities of copper, lead, zinc, etc. For copper and zinc, volumes of from one drop to 10 c. c. are evaporated to dryness, moistened with dilute nitric acid, evaporated to dryness, taken up with a drop or two of distilled water, and a portion of this liquid tested upon an object slide with ammonium mercuric sulphocyanate. In the case of lead the water is treated exactly as above and the lead made evident by the usual triple nitrite reaction, using cesium chloride to hasten the

forming of the crystal phase. The crystals obtained in these cases are abundant, well formed, very characteristic, easily recognized, and not liable to any serious interferences by other substances which may be present.

With two microscopes available and a comparison eyepiece, quantitative colorimetric methods can be employed with minute quantities of water and yet with an accuracy comparing very favorably with our standard methods of water analysis. This is a matter of vital importance when the taking of very small samples of water only is practicable.

In this short résumé I have endeavored to point out that microscopic methods are capable of a very broad application, permitting us to study not only organisms included in the general term of plankton but also enabling us to estimate the bacteria present with ease and rapidity, and to make qualitative or even quantitative analyses with an economy of time, material, and space not possible by any other method, and more important still, that the microscope intelligently employed yields information of a character of prime importance and inestimable value in the sanitary examination of water and even in the operation and design of water-filtration plants.

The CHAIRMAN. Dr. Edward Bartow, director State Water Survey, Urbana, Ill., is the next on the program.

THE SIGNIFICANCE OF CHEMISTRY IN WATER PURIFICATION.

By EDWARD BARTOW,

Director State Water Survey, Urbana, Ill.

When water purification is mentioned one thinks first of water for drinking purposes. It is a fact, however, that a very small percentage of the water furnished by a municipality to its citizens is used for drinking purposes. Water purification must include treatment of water for drinking purposes, for domestic uses, for the production of steam, and for manufacturing processes. The value of an abundant supply of pure water for all purposes is becoming more generally realized, and many investigators have been and are endeavoring to find the best means for judging the quality of a water and for purifying water. The chemist, the bacteriologist and the biologist are all busy investigating these problems.

The bacteriologist rightly considers that the presence or absence of disease-producing bacteria is the only absolute means of judging whether a drinking water will cause disease. But the difficulties in determining absolutely the presence or absence of disease-producing bacteria and the uncertainty which negative results leave with regard to possible later access of pathogenic bacteria make it necessary to use some index other than the disease-producing bacteria themselves by which to judge the purity of a drinking water. The bacteriologist has the nearest approach to a reliable index in the bacteria which accompany pollution. Bacteria of the colon group are always present in sewage, and their presence or absence in a drinking water is very important since it implies the presence or absence of pollution by sewage. Therefore, finding the colon bacillus, the bacteriologist would condemn the water. The biologist, finding organisms that impart an unpleasant taste or odor, would condemn a water. The sanitary inspector, from a survey of the territory surrounding the source of a water supply, finding unfavorable conditions, would condemn a water without further examination. The bacteriological, biological, and inspection approval of a water is not sufficient. Chemical approval in addition is necessary because of the possibility of unseen underground contamination, because chemical tests reveal the previous history of a water and may indicate possible future contamination, because chemical tests determine the therapeutic character of a drinking water.

Chemical tests are used to determine the purity of water and to control the treatment. Chemicals are used in purification and disinfection of water supplies.

When it was first realized that a polluted well water might spread infectious diseases chemical tests alone were relied upon by the water analyst. Because organic waste matter contains nitrogen as an important constituent, Wanklyn in 1868 first suggested the determination of nitrogen as an index of the character of a water supply. He proposed the albuminoid ammonia test and while it has had considerable criticism it has, nevertheless, served a good purpose. The albuminoid ammonia test and the determination of oxygen consuming capacity have given the best information concerning the character of a water supply, until the introduction of bacteriological tests. For many years the sanitary examination of a drinking water consisted of purely chemical tests and included the determination of residue, chloride, oxygen consuming capacity, free ammonia, albuminoid ammonia, hardness, dissolved gases and poisonous metals. Later, owing to the demand for a clearer water free from iron and manganese, determinations of alkalinity, carbondioxide, iron and manganese were added.

When bacteriological tests are made, it is surprising to note the amount of chemistry used by the bacteriologist. Even in determining the number of bacteria, the acidity of the media must be accurately adjusted by chemical analysis. The determination of the colon bacillus, as stated before, the most reliable index of pollution, depends upon the chemical decomposition of sugars in media whose acidity is accurately adjusted. Other tests for the colon bacillus depend upon the chemical reaction toward litmus lactose agar or Endo's media. The formation of indol and its recognition are chemical reactions used by the bacteriologist.

At present in the analysis of drinking waters certain chemical tests may be said to supplement the bacteriological tests. These are the tests for organic matter. They include tests for ammonia, albuminoid, nitrite, and nitrate, nitrogen, and the oxygen consuming capacity.

The inorganic constituents must not be overlooked. Some serve as an index of pollution, others have therapeutic significance. Chloride furnishes an example of the usefulness of a chemical test as an index of pollution. It is always present in sewage, hence in regions where the amount of chloride present in normal waters varies with the distance from the sea coast an excess of chloride above the normal arouses suspicion. It must be remembered, however, that in other regions, especially regions which have been covered by the sea, the normal chloride of the water supplies is so high and its variation so great that it is impossible to use it as an index of pollution. The chemical analysis of the inorganic soluble matter shows the therapeutic significance. Waters containing notable amounts of the sulfates of sodium, or magnesium, or waters containing dissolved gases, especially hydrogen sulfide, will have a physiological action on those who drink them, especially on those who are not accustomed to them. Therefore, these waters containing large amounts of sulphates or hydrogen sulphide are valuable mineral waters.

The chemical tests for the troublesome metals, iron and manganese, and the poisonous metals—copper, lead, and zinc, must not be overlooked. Copper, lead, and zinc are found in waters in mining regions and many waters will dissolve lead or zinc from pipes. The drinking of these waters will cause serious illnesses. Iron and manganese if present in sufficient quantity to be injurious are usually precipitated on contact with the air and give warning against the use of the water.

To determine definitely the therapeutic value of a water accurate determinations of the chemical composition of the mineral content of waters are needed. These accurate determinations serve also to show the value for use in boilers, for manufacturing purposes and for the determination of methods of water purification. The tests ordinarily made are for the positive ions, potassium, sodium, iron, aluminium, calcium, magnesium, and for the negative ions, chloride, nitrate, sulfate, and car-

bonate. Sometimes rare ions such as bromide, iodide, lithium, and phosphate are determined. For boiler use an excessive amount of calcium and magnesium will cause the formation of scale. Chloride or nitrate ions in excess will cause corrosion and sodium and potassium in excess will cause foaming. Many examples might be given of the injurious action of soluble compounds in water used for manufacturing. Suffice it to say, that compounds of iron and manganese by their color interfere with bleaching processes; calcium and magnesium increase the amount of soap required and form substances that can be with difficulty removed from fabrics, thus interfering with laundry processes; calcium and magnesium when present in water used in preparing foods give an inferior product.

Chemists have been working for years to improve methods of analysis and methods of purification. They have been working in cooperation on methods of analysis and individually on methods of purification. In the United States committees have formulated standard methods of analysis. The first attempt to obtain uniform methods was made by the chemical division of the American Association for the Advancement of Science, which presented a preliminary report at the meeting in Cleveland in 1886.[1] This committee gave standards for (1) free and albuminoid ammonia; (2) oxygen consuming capacity; (3) nitrites; (4) nitrates, and implied that residue, chloride, and hardness should also be determined but gave no specific directions for these tests. The American Public Health Association in 1894 took its first step toward the formulation of standard methods.[2] The committee formed at that time made several progress reports and prepared recommendations for bacteriological examination of water. It was not until 1905 that they published the first report on standard methods of water analysis, including both chemical and bacteriological methods. A revised report was published in 1912 and a second revision will appear during 1916. This published report on Standard Methods has done much to unify the chemical procedure in water laboratories and to promote interest in investigation of methods of analyses.

Having by analysis found a water impure the next step is purification. The method of purification depends upon the proposed use. Drinking water demands filtration to remove turbidity and bacteria when waters are turbid. Impure drinking waters, if clear, demand disinfection. Slow sand filters, imitating nature's process were first used to remove turbidity and bacteria. Owing to the expense of installation, especially in America, the so-called mechanical filters have been substituted. Chemicals are necessary for the operation of mechanical filters. By means of chemicals a precipitate is formed, which in settling collects colloids and bacteria and permits the water to be filtered at nearly 40 times the rate possible when no chemicals are used. Aluminium sulfate (filter alum) iron sulfate, and lime separately or in combination, are the chemicals added. Aluminium sulfate reacts with the bicarbonates of calcium and magnesium in the water to form a precipitate of aluminium hydroxide. Iron sulfate usually added with lime reacts with the bicarbonates of calcium and magnesium to form a precipitate of iron and magnesium hydroxides, and calcium carbonate. It is necessary to add sufficient lime to neutralize any free carbon dioxide present or set free by the iron sulfate. Lime reacts with magnesium salts forming a sufficient precipitate to allow filtration without aluminium or iron sulfate or with a very little of either to counteract the excess of lime. Waters with an excessive turbidity like those in the Mississippi River Valley, can not be filtered practically by slow sand filtration and filtration with chemicals is used exclusively.

Each year the public is demanding better water. Standards of purity are being raised. The United States Public Health Service, through a commission, has formulated standards for the purity of drinking water to be used on interstate carriers.[3] A glance at the literature of the last few years shows how investigators are endeavoring

[1] The Journal of Analytical Chemistry, 3, 398 (1887).
[2] Proceedings of the American Public Health Association, 20, 81 (1894).
[3] Public Health Reports, 29, 2959 (1914).

to comply with the demand for better water. It is difficult to conform to the improved standards for drinking water without disinfection.

For disinfection, ozone, ultraviolet rays, bleaching powder, liquid chlorine and lime are used. Ozone has been used quite extensively in Europe. Plants are in operation in Europe at Wiesbaden, Schierstein, Paderborn, Cosne, Chartus, Nizza, Dinard, Sulina, Ginnekin,[1] St. Maur,[2] Chemnitz, Florence, Spezia, Genoa, Braila, Paris,[3] Koenigsberg,[4] Petrograd[5] and other places.

The plants which have been constructed in the United States [6] have not been very successful and it must be considered that the use of ozone in America is still in the experimental stage.

Disinfection or sterilization with the ultraviolet ray was first proposed by Henri, Helbrunner, and Recklinghausen.[7] Their pioneer work has been followed by many investigators. Plants are in operation in Europe at Luneville, St. Malo, and Rouen.[8] No large installations have been made in the United States but small installations have been used with evident success.

Bleaching powder (calcium hypochlorite) was first used in 1908 at the Union Stock Yards in Chicago and at the Boonton Reservoir of the Jersey City supply. The process because of its cheapness is being widely used throughout the United States. In 1915 Longley [9] reported that 240 water supplies were being treated with some disinfecting agent; about 80 per cent using bleaching powder and the remainder liquid chlorine.

Within the last few years liquid chlorine has been made available and several forms of apparatus for adding liquid chlorine to water have been successful. It is much easier to handle the liquid chlorine or the gas from it than to handle the bleaching powder. This method will very soon replace the use of bleaching powder.

Investigations by Houston [10] in London have shown that the addition of lime before storage of water removes the bacteria almost completely. Sperry at Grand Rapids and Hoover [11] at Columbus have shown that a slight excess of lime when used as a precipitant removes the bacteria, serving as an excellent disinfectant. For the disinfection of drinking water on a small scale potassium permanganate, bromine, iodine, and bleaching powder have been used. Tablets of bleaching powder with tablets of sodium thiosulfate to remove the excess of bleaching powder are quite satisfactory. In brief this is the summary of chemical methods of purifying drinking water.

For purifying water for the production of steam and for manufacturing processes or "water softening," lime and soda, alone or in combination have been long used. Lime is used for the removal of carbonates; soda for the removal of sulfates, nitrates and chlorides of calcium and magnesium. Soda may be replaced by other sodium salts so that sodium silicate, sodium phosphate, sodium hydroxide, etc., are used in water softening and boiler compounds.

A new method for softening water was suggested by Gans.[12] It had been known that zeolites would soften water but since a sufficient quantity of the natural material could not be obtained Gans prepared an artificial zeolite by fusing kaolin, feldspar soda, and potash. This artificial zeolite called by the trade name "permutit," has the power of removing calcium and magnesium from a hard water, delivering a water

[1] Ed Imbeax Wasser u. Abwasser, 7, 39. (1915.)
[2] R. Spaulding Eng. Mag. 45, 725. (1913.)
[3] G. Erlwein Gesundh Ing. 36, 17. (1913.)
[4] K. Kisskalt Gesumdh Ing. 38, 195. (1915.)
[5] F. P. Mann Mun. J., 32, 935. (1912.)
[6] S. T. Powell, J. Ind. Eng. Chem. 6, 959 (1914). M. W. Franklin, J. Ind. Eng. Chem. 6, 959 (1914). S. T. Powell, J. N. W. W. Assn. 29, 87 (1915).
[7] Compt. Rend, 155, 852. (1915.)
[8] Recklinhausen, J. Am. W. W. Assn., 1, 565. (1914.)
[9] Longley, J. Am. W. W. Assn., 2, 679 (1915).
[10] Houston, 8th Research Report Metropolitan Water Board, 1912. J. Soc. Chem. Ind., 31, 508. (1912.)
[11] Hoover, Eng. Record 68, 257. (1913.) Sperry, Mun. Eng., 45, 343. (1914.)
[12] Gans, Chem. Review, Fett-Harz Ind., 16, 300 (1909). Chem. Ind., 32, 197.

with zero hardness. The process is well adapted to soften water for the textile industry, for laundries, etc. Only one municipal plant, at Hooten, England, has been built. As yet it seems too expensive for municipal water supplies but very probably efforts will be made to lessen construction costs so that it can be made available for municipalities.

The use of disinfectants and the invention of permutit are the most important recent improvements in water purification. Many other improvements of minor importance but having practical value have been recently discovered. Copper sulfate[1] has been found to be an efficient algæcide and is widely used to remove algae growths from reservoirs. Alum has been made from sulfuric acid and bauxite[2] and without refining has been used at Columbus, Ohio, in water purification with a great reduction in the cost of purification. In Omaha[3] the efficiency of filter alum is said to be greatly increased by passing the solution of alum over iron filings before adding it to the water to be purified. Analyses of chemicals and their purchase under specifications has increased the efficiency of water purification plants.

A summary of this paper on the "Significance of chemistry in water purification" should answer the question often asked: What does water chemistry do?

It assists in and supplements bacteriological tests.

By determining the mineral content of a water; it shows the therapeutic character; it shows the presence or absence of troublesome metals, iron and manganese; it shows the presence or absence of poisonous metals, copper, lead, and zinc.

It controls purification.

It formulates standards of purity and improves methods of purification.

It makes filtration of turbid water possible.

It softens water for many purposes.

Finally, its fundamental purpose is to furnish and conserve pure water for all purposes.

The CHAIRMAN. You have heard the papers on "Water Supply." I would like to ask Prof. Bartow if there are plants in this country that have the dual water supply, such as they have in some European cities where there is drinking-water service and also commercial-water service.

Dr. BARTOW. Mr. Chairman, I am unable to answer that question. It is my understanding that in New York City they have along the water front hydrants through which they can pump water for fire protection.

The CHAIRMAN. I mean general, throughout the city.

Dr. BARTOW. I do not know of any such plant.

Dr. SEDGWICK. I have greatly enjoyed these papers, and I think that Prof. Bartow's survey of the situation as to both chemical and bacterial analysis is thoroughly admirable and very helpful. I remember the time, however, when by chemical analysis highly polluted waters were allowed to be drunk, because we did not then have the notion of the bacterial content; when, for instance, the Merrimac River at Lowell, because it analyzed well chemically, was reputed to be good for drinking. Of course that is many years ago, but it was done at the hands of excellent chemists. It has greatly

[1] Moore and Kellerman, Bul. 64, Bureau of Plant Ind., U. S. Dept. Agriculture.
[2] Hoover, Eng. News, 72, 1239 (1914.)
[3] Jacobson, Eng. Record, 71, 394 (1915).

strengthened the bacterial side to be able to bring in or to secure the aid of the chemists, and I think the bacterial side in its turn has done something for the chemists. Certainly no bacteriologist or biologist would ever claim that his science is anything more than the chemistry and physics of living matter, and biologists and bacteriologists always rejoice to hear of the progress which is being made in chemistry. We know what the water survey of Illinois has done to help us in these various directions.

One point in Prof. Jordan's paper interested me very much, and that was his dealing with the so-called Mills-Reincke phenomenon when that was emphasized some years ago and Hazen's theorem was formulated. Some of you may not know what these things were, but the gist of them was this, that for every death from typhoid fever saved by the purification of the water supply, two or three deaths from other diseases were likewise saved, and this numerical relation was named Hazen's theorem. That was submitted with a good deal of diffidence by the authors, who said that it seemed to be accounted for by one of two things: Either there were some organisms capable of carrying diseases in water which were not at that time recognized as thus capable (tuberculosis, for example), or else that the vital resistance of people was affected unfavorably by polluted water. Neither explanation seemed then wholly satisfactory, but the former has some support to-day. In the meantime various critics of the findings have arisen, notably Dr. Chapin, the admirable authority at Providence, who, however, is always skeptical of everything that is not strictly proved, and the hardly less well-known Dr. Houston in charge of the London water supply. There appeared, however, in January last—I think it was—the paper by Dr. Dublin, which was referred to by Prof. Jordan, in which the experience of an insurance company with typhoid convalescents was recorded with respect to their susceptibility to other diseases, and while the paper can hardly, perhaps, be considered as final or conclusive, it was very interesting as far as it went, for it said, as Dr. Jordan stated, that typhoid recoveries seem to be, so to speak, comparatively temporary, dying of other diseases before very long, or at least before others in the same group who had not had typhoid. Col. Woodruff, the author of "Tropical Life," who has studied the effects of tropical life on the white man, was also very much interested in this matter, and he had figures which seemed to him to show that people having had typhoid were more than ordinarily susceptible to tuberculosis, etc.

Dr. GEORGE A. SOPER. With respect to the amount of protection afforded—referring to the fact stated by Prof. Jordan that about 80 per cent of the population of this country is supplied with pure water—I think we should not come to the conclusion that the protection against typhoid is quite as great as the figure 80 per cent

would indicate. We must know more of the 20 per cent of the unprotected and the means by which they may communicate the disease.

The introduction of a pure water supply does not always reduce the typhoid rate so much as is expected. We have an instance in the city of Washington, where the introduction of an improvement in the existing water supply was expected to practically eliminate typhoid fever. Very much to our surprise there was little, if any, reduction in typhoid.

Throughout several cities apparently somewhat similar surprises have resulted, and we must, I believe, recognize that diseases which we have formerly been taught to regard as transmitted chiefly if not exclusively, through water are also transmitted through other vehicles. It has within the last few years come to be regarded in England that contact infection, for example, in typhoid fever plays a predominant, if not exclusive, rôle in producing high death rates from typhoid fever.

We should consider these matters chiefly from the standpoint of the latest information which investigators can give. Such work as the United States Public Health Service has done in Washington should by all means be reinforced, indorsed, and the proof supplemented, so that no doubt shall remain as to the means by which these so-called water-borne diseases are to be controlled.

Dr. KOBER. It may be of interest to the advocates of the water-borne theory of typhoid fever that the history of Washington shows clearly that when we had local pump supply and polluted water supply from the Potomac River there was an ever-increasing rate from year to year. In 1889 to 1890 we had a typhoid rate of 104 per 100,000 of population. It was during that year that I dared to assert that the typhoid fever epidemic at Cumberland, Md., would react upon our typhoid fever rate. My suspicion that typhoid fever germs discharged with sewage into the Potomac River at Cumberland, a distance of 134 miles away, might infect consumers of Washington was confirmed by studying the effects of the Cumberland epidemic upon the prevalence of the disease in Washington. The records of the Health Office show that during this epidemic from December, 1889, to April, 1890, the deaths from typhoid fever amounted to 74 as compared with 42 for the corresponding months of the previous year. Indeed we had almost double the number of typhoid deaths during these months than for any similar period either before or since this epidemic. It was the fact of calling attention to this coincident event, and also simultaneously the demonstration made by Dr. Theobald Smith that turbid water always contained a large number of colon bacilli, that actually aroused an interest in the typhoid fever situation and the purification of the water. Steps were taken to increase the storage facilities of the water supply of Washington,

permitting of longer sedimentation; city pumps and box privies were gradually abandoned and with these improvements there was a decided reduction from year to year in the prevalence of typhoid fever.

One of the great factors before filtration was actually adopted was the installation of a reservoir which permitted longer storage for our water, and everyone familiar with the subject knows that sedimentation alone will eliminate about 87 per cent of bacteria. So that we really had a marked decrease in typhoid fever before the actual completion of the filtration plant, but for the information of the last speaker I will say that it is a very different thing to compare a typhoid-fever rate of 104 per 100,000 of population in 1890 and one of about 15, which we have at the present time. I feel no hesitation in declaring that over 50 per cent of all the typhoid-fever cases in this city before the completion of the system of water purification were water borne, and this in spite of the fact that I was a pioneer on the subject of milk-borne typhoid and also the first man on record in this country to direct attention in 1895 to the agency of flies in the transmission of typhoid fever. Those who are interested in the subject will find a very excellent chart prepared by me in Rosenau's recent book on hygiene, in which the very important rôle which polluted waters play in the transmission of typhoid fever is conclusively demonstrated.

Dr. BARTOW. Prof. Sedgwick has spoken of the water which was formerly allowed to be used because of its supposed purity after chemical tests were made. I want to tell of one which was condemned because of the chemical tests, although it was bacteriologically pure. The central part of Illinois was once covered by glaciers. The water is drawn from depths of 150 to 200 feet from gravel stratum that contain a large amount of nitrogenous organic matter.

The waters are unfit for drinking purposes, and water from our wells has been condemned by one of our best Illinois authorities on the ground that the free elements were too high, whereas when we analyzed this water bacteriologically it was practically sterile.

With regard to the reduction of typhoid fever by the introduction of water supply, one of the greatest steps in this direction has been the introduction of a filter plant at Niagara Falls. The typhoid rate in that city used to be 160 to 170 per 100,000. After the introduction of that plant, the typhoid rate dropped, I think, to 15, or something like that, and one can hardly conceive what improvement that meant in the conditions all over the country, as so many people visit Niagara Falls.

The CHAIRMAN. If there is no further discussion of the papers we have heard, the next on the program is that of Dr. Allan J. McLaughlin, United States Public Health Service, on the subject of "The control of Asiatic cholera along international trade routes."

THE CONTROL OF ASIATIC CHOLERA ON INTERNATIONAL TRADE ROUTES.

By ALLAN J. McLAUGHLIN,
United States Public Health Service, Commissioner of Health, Massachusetts.

General principles of control of Asiatic cholera on international trade routes are the same for overland travel as for travel by sea. These principles demand the restriction of travel to certain definite routes which pass, at the frontier or on the sea coast, through well-equipped modern quarantine plants.

LAND ROUTES.

An international trade route overland may involve several kinds of transportation, and the character of the transportation is a matter of vital importance in the spread of Asiatic cholera. Asiatic cholera spreads as fast as man can travel, so that it can not spread as fast along a caravan route as along an international railroad line.

THE ESTABLISHMENT OF FRONTIER QUARANTINE STATIONS.

When a country is menaced by Asiatic cholera on its land frontier, whether the routes over this frontier are caravan routes, ordinary roads, or railway lines, passage of the frontier must be prevented, except at certain specified quarantine stations. In the interests of commerce and passenger traffic, these stations should be established on all important points through which passenger or freight traffic ordinarily crosses the frontier.

These quarantine stations or detention camps on a frontier should not be essentially different from the regular maritime quarantine stations which are used to protect against Asiatic cholera carried along sea routes, and for that reason the same type of quarantine station will serve for either land or water quarantine.

WATER ROUTES.

Lanes of ocean travel are almost as definite as roads for land travel, and great steamship lines run on a schedule with the regularity of railway trains. These great steamship companies use regular terminals in the large seaports, and their control is no more difficult than that of regular train traffic on land. There are in addition tramp steamers and sailing vessels. These present less difficulty than irregular traffic across a land frontier. Similarly, water routes by river or canal are controlled by a quarantine station at the frontier.

Just as in the case of land frontiers, the seaboard of a country may be closed except certain specified ports, provided with proper quarantine stations, through which all traffic must pass. In the interest of commerce this list of open ports should include all important ports, and as many smaller ports at which quarantine stations can be maintained at a cost commensurate with the importance of the port.

THE ESSENTIALS OF SUCCESSFUL QUARANTINE.

The essentials of successful quarantine are the same on land and sea, and include:

1. Accurate information and delimitation of the infected territory.
2. Efficient facilities and personnel for inspection at the seaports or points on frontiers where important roads or water routes cross the frontier.
3. Modern quarantine stations.

It is not possible within the limits of this paper to discuss all the details of these essentials. I will omit discussion concerning the very interesting and sometimes devious methods by which information is secured, and of the problematical value

of so-called official information. I shall be obliged also, because of lack of space, to omit detailed description of what constitutes an efficient equipment and personnel of an inspection service, and of a modern quarantine station.

I should like to accentuate the necessity of giving the menaced country the benefit of the doubt in attempting to delimit the infected zone in a neighboring country, and to bring out certain important changes of technique and procedure in the handling of an Asiatic cholera quarantine.

DELIMITATION OF INFECTED TERRITORY.

The delimitation of infected territory is of the utmost importance, but it is often extremely difficult to secure accurate information of the exacta rea which may be classed as infected. It is a very dangerous procedure to assume that certain portions of a country are cholera free, unless a representative of the menaced nation is on the spot, whose investigations are unhampered, and whose reports are uncensored. In 1905, for example, it was claimed that northern Russia was free from Asiatic cholera, while southern Russia was infected. The writer was on duty in Hamburg, Germany, at the time and recommended that all Russia be considered infected, in view of the fact that all trains crossing the German border must pass through infected territory either in Poland or the valley of the Vistula, and that owing to internal disturbances in Russia, the Russians themselves were unable to delimit accurately the infected area. This was the attitude of the German Imperial Health Office, and the United States sustained its representative, ordering that all Russians be detained in quarantine under observation in German ports, before embarking for United States ports.

On the other hand, in Germany, because of unhampered investigation and ready access to accurate information, and also the uncensored use of the cable, it was possible to delimit the infected area and to remove restrictions from a large part of the empire. While the importance of exact delimitation in avoiding undue restriction can not be overestimated, it is nevertheless wise to err on the side of safety, and a country menaced by Asiatic cholera is justified in imposing its quarantine restrictions upon suspected, as well as infected, territory.

PERIOD OF DETENTION IN QUARANTINE.

Formerly cholera quarantine detention was at least five days, and this period of five days under observation was considered a sufficient guaranty for safe discharge from quarantine, provided no signs of illness developed. In the Philippines, in 1908 and 1909, the writer, as a requirement for discharge of contacts from quarantine, substituted a negative examination of the intestinal discharges for the ordinary five-day detention period.

In October, 1910, the writer recommended to the Surgeon General that the intestinal discharges of all arrivals at United States ports from territory infected or suspected of being infected with Asiatic cholera, should be examined bacteriologically, and that discharge from quarantine be made only after a negative result of the stools examination. On July 19, 1911, the Secretary of the Treasury promulgated a regulation providing for this additional safeguard.

The demonstration of carriers who discharged vibrios in their stools for weeks, and even months, showed that no mere arbitrary detention alone could prevent their passage through quarantine.

Rapid methods of technique and an efficient system of collecting samples and handling the specimens make it possible for each bacteriologist to examine 100 to 150 stools per day.

This important advance in our methods of Asiatic cholera quarantine not only gives us an additional safeguard in preventing the entrance of vibrio carriers, but makes possible the shortening of the period of detention from five days to two or three days.

TECHNIQUE OF BACTERIOLOGIC EXAMINATION OF STOOLS ON A LARGE SCALE AT QUARANTINE STATIONS.

In considering the problem of a stools examination on a large scale, two factors must be given their proper weight:

1. Proper protection of the public.
2. Minimum restriction of commerce consistent with No. 1.

If we could take unlimited time in the matter we would use every procedure known for the detection of the cholera vibrio, and would probably detain the suspects in quarantine many days or weeks, but as quarantine officers, we are charged by law with carrying out the quarantine regulations, and especially instructed to carry them out with the minimum restriction of commerce. This necessitates the elimination of hanging drop or other slow technical procedures, cholera red reactions, use of gelatine media, and many other tests which are interesting, but not necessary for cholera diagnosis and only serve to increase the time of the examination.

SECURING THE SPECIMEN.

The specimen is best secured by the administration of a saline, and magnesium sulphate serves very well. It is best administered on an empty stomach about 6 a. m. Suspects with diarrhea and children may be exempted, and a good specimen may be obtained from these by passing a large catheter or rectal tube with several "eyes" cut in the upper end. In withdrawing the tube the "eye" scrapes mucus off the lining of the bowel and furnishes a very good specimen. The use of swabs is not recommended, as a good specimen is difficult to obtain if the suspect is constipated. The swab has a great deal of the material scraped off by the tight sphincters and further may cause considerable pain and injury, especially when hemorrhoids are present. Dr. Serrati, the Italian royal commissioner at New York, suggested that the swabs be sheathed in glass tubes. The tube protects the swab in passing the sphincters and is also less painful in passing.

DISPOSAL OF THE STOOLS AFTER PLANTING.

The specimen should be passed in a paper sanitary cuspidor or similar receptacle which is cheap and may be burned. After planting in peptone the stool and container is dropped in a flour barrel. When the barrel is full or the samples all taken the cover is placed and the barrel with its contents burned.

The specimens are planted in peptone by means of sterile pieces of wood (an ordinary wooden tongue depressor split in three serves very well). This obviates the necessity of sterilizing a platinum loop or other metal instrument and saves much time. After planting, the stick is destroyed with the specimen in the barrel.

PLANTING AND RECORDING THE SPECIMENS.

The suspects are divided into groups of 150 to 200, each group designated by different-colored tags. The plants are made on a table convenient to the latrines. The specimens are brought to the bacteriologists at the tables by the male suspects themselves, under the supervision of orderlies or male nurses. The specimens from the women and children are taken by trained female nurses and brought to the tables. At each table there is, besides the bacteriologist, a clerk, who records the name of the suspect in a book and gives him a number in consecutive order. This number goes on the suspect's colored tag and also on the peptone tube, which has been inoculated. The amount of material for each peptone tube should be about equal to two or three large loops. After inoculation the tubes should not be agitated, and agitation should be avoided until the smears are made after incubation.

INCUBATION.

The best temperature for incubation is from 35° to 37° C., and the tubes should be incubated about six hours. If it is not possible to examine before eight hours, second peptone subcultures should be made.

MAKING SMEARS AND STAINING.

To make a satisfactory smear from a peptone culture is not easy. Four or five large loops from the surface (but avoiding the pellicle) are placed in the center of a clean slide, and without much spreading dried slowly and fixed by heat. This gives more concentration and more organisms in a field than if one drop was spread upon a slide. The stain should be carbol-fuchsin 1 part diluted by the addition of 9 parts of water. Stain about one minute, wash carefully, and examine. It is convenient to have the numbers cut on the slides with a diamond, numbering the slides consecutively, in lots of 50, as the peptone cultures come in in racks of 50. The slides corresponding to the numbers on the tubes were selected and used.

EXAMINATIONS OF THE SMEARS.

This is the most important step in the technic. If carelessly done, the whole examination is valueless. If properly done, 80 to 90 per cent of the specimens may be rejected without plating. The observer must search, using a mechanical stage, from 25 to 50 fields, and if he finds no suspicious curved organisms, the specimen is marked "negative." If he finds curved organisms, a subculture in peptone and plates are made. To be able to do this requires acute vision, and a knowledge of vibrios and other curved forms. The observer at first finds curved organisms in nearly every specimen, but after plating these out he finds that many are not vibrios at all. At first the beginner will plate out about four-fifths of his specimens. After training and the experience gained by studying his plates, he will not find it necessary to plate more than 10 per cent. The differentiation of what seem to be curved organisms and vibrios can only be learned by actual experience, and safety at first lies in plating all the doubtful ones.

PLATES.

The plates should be ordinary nutrient agar (2 to 3 per cent) neutral to phenolphthalein, the surface dried an hour in the thermostat at 37° C., or one may use plates more than 24 hours old. The plates should be examined after about 16 hours.

AGGLUTINATION TESTS.

The colonies which have the characteristics of the cholera colonies may be fished direct to drops of 1 to 200 specific cholera serum on a clean glass slide, carefully marking the colony on the plate. Or a smear may be made from the colony, stained, and examined. In any event, the colony, if a vibrio, must be fished to an agar slant grown 18 hours and a quantitative agglutination made, using a serum of a titer of at least 1:4000 in dilutions ranging from 1:50 to 1:1000. Dilution 1:1000 should be positive beyond question after one hour in the incubator at 37° C.; 1:200 should give an instantaneous agglutination. The agglutination test should be controlled by test with a known cholera vibrio and with dilutions of normal serum and salt solution.

The rapid test on the slide with an instantaneous reaction in a dilution of 1:200 may be completed by drying, fixing, and staining the clumps in situ. Under a low power the clumps will show very well, and the higher-power lenses will show the characteristic morphology.

IMPROVEMENT IN MEDIA.

One other advance in our methods of handling Asiatic cholera suspects has been made by Goldberger,[1] which promises to increase our efficiency in detecting Asiatic cholera carriers when making stool examinations on a large scale.

There has been no great change in the bacteriologic methods of Asiatic cholera diagnosis in the past 10 years, and these methods are based upon the procedure of the German Imperial Health Office.

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[1] Goldberger, Joseph, Some new cholera selective media. Hygienic Laboratory, Bulletin No. 91, Washington, 1914.

As a time-saving measure, test tubes are used instead of large flasks for the peptone solution. This necessitates that the amount of feces added to the tube must be small, and if the vibrios are very scarce a carrier might be recorded as negative. Large flasks and many platings are impracticable on a large scale where the daily examinations may run in thousands. Goldberger's media permits the planting of relatively large quantities of feces, using the same convenient size of test tubes.

Goldberger suggests two enriching solutions, an alkaline egg peptone and an alkaline meat infusion peptone. The cholera vibrio grows well in both solutions, though less luxuriantly than in ordinary cholera peptone. The multiplication of the ordinary fecal bacteria is markedly restrained, especially the colon bacillus. Goldberger's work shows that in his media the vibrios, if present even in small numbers, will increase and not be overgrown, even after 72 hours. Goldberger's media was devised after a careful study and test of the various selective media suggested by Dieudonné, Newfeld and Woithe, Esch, Pilon, Crenderopoulo and Panayotatou, Krumwiede, Pratt and Grund, Hoffmann and Kutscher, Moldavan, and others.

The addition of Goldberger's media to our equipment should make the passage of an Asiatic cholera carrier through our quarantines still more unlikely. It is true that this media has not yet been tested in actual field work, but the laboratory tests suggest that it is the most valauble addition to our cholera technique which has been made in recent years.

CONCLUSIONS.

1. The spread of Asiatic cholera in international traffic is largely a question of the travel of cholera carriers.

2. Frank cases of cholera present no difficulty in diagnosis, can not travel fast or far without detection, and consequently should be considered a lesser menace by the quarantine officer than the carrier without symptoms.

3. An arbitrary period of detention in days is not a sufficient safeguard per se but should only serve as an opportunity for detecting cholera in the intestinal contents of the suspects.

4. Model quarantine stations upon all trade routes by land or sea, where they cross the frontier or at their seaport terminals, are a necessity, and in times of danger all travel from infected territory should be restricted to routes thus equipped and controlled.

5. The most important feature of a model quarantine station should be the laboratory equipped to examine and report on not less than 100 stools per day for each bacteriologist.

The CHAIRMAN. Dr. C.-E. A. Winslow, Yale University, New Haven, Conn., will now present a paper on "Fresh air and ventilation in the light of modern research."

FRESH AIR AND VENTILATION IN THE LIGHT OF MODERN RESEARCH

By C.-E. A. WINSLOW.

Anna M. R. Lauder Professor of Public Health, Yale Medical School, and chairman, New York State Commission on Ventilation.

The problems of ventilation might at first sight appear to be of so universal a nature as to have but little place in the program of a conference largely devoted to the comparative problems of the different countries on our hemisphere. Normal air has indeed the same percentage chemical composition wherever we may sample it.

Altitude, however, strikingly affects physiological reactions by its influence on partial pressure; and the extension of our conception of air conditioning to include a consideration of the physical effects of the atmosphere upon the body brings the whole question of temperature and humidity and climate within its scope.

The evil effects of bad air conditions are obvious and clearly recognized. In a crowded, ill-ventilated room we experience a feeling of dullness, sleepiness, and under more extreme conditions perhaps nausea, and even faintness; and there are several classic instances in which conditions of the atmosphere have become so extreme as to result fatally. The most famous of these examples is the Black Hole of Calcutta, which Prof. Lee, of Columbia University, has described in the following sentences:

On one of the hottest of the hot nights of British India, a little more than 150 years ago, Siraj-Uddaula, a youthful merciless ruler of Bengal, caused to be confined within a small cell in Fort William 146 Englishmen whom he had that day captured in a siege of the city of Calcutta. The room was large enough to house comfortably but two persons. Its heavy door was bolted; its walls were pierced by two windows barred with iron, through which little air could enter. The night slowly passed away, and with the advent of the morning death had come to all but a score of the luckless company. A survivor has left an account of horrible happenings within the dungeon, of terrible strugglings of a steaming mass of sentient human bodies for the insufficient air. Within a few minutes after entrance every man was bathed in a wet perspiration and was searching for ways to escape from the stifling heat. Clothing was soon stripped off. Breathing became difficult. There were vain onslaughts on the windows; there were vain efforts to force the door. Thirst grew intolerable, and there were ravings for the water which the guards passed in between the bars, not from feelings of mercy, but only to witness in ghoulish glee the added struggles for impossible relief. Ungovernable confusion and turmoil and riot soon reigned. Men became delirious. If any found sufficient room to fall to the floor, it was only to fall to their death, for they were trampled upon, crushed, and buried beneath the fiercely desperate wave of frenzied humanity above. The strongest sought death, some by praying for the hastening of the end; some by heaping insults upon the guards to try to induce them to shoot. But all efforts for relief were in vain, until at last bodily and mental agony was followed by stupor. This tragedy of the Black Hole of Calcutta will ever remain as the most drastic demonstration in human history of the bondage of man to the air that surrounds him.

On the other hand, the beneficial effects of good air are equally susceptible of demonstration. Dr. Edward Trudeau, who died November 15 last, went to Saranac in 1873 as a hopeless victim of consumption. All his friends were filled with horror at the idea of his going practically alone to die, as they believed, in the Adirondack wilderness, in a little town consisting of little more than a sawmill and half a dozen cabins, 42 miles from a railroad. Dr. Trudeau did not die during the winter of 1873, but grew very much better; and some 10 years later, as a result of his experience, he founded the Adirondack Cottage Sanatorium, which in its primitive form consisted of a single house in which, with great difficulty, he persuaded two consumptive patients to live. That was the beginning of the demonstration in this country of the fresh-air treatment of tuberculosis, which Brehmer and others had introduced on the other side of the water. To-day we are going through a reaction against the more extreme applications of very cold air to sick people and to infants; but the general value of fresh air, if not too cold, and except in certain diseases, has been amply demonstrated.

What are the factors to which these evil effects of bad air and these beneficial effects of good air are due?

The air is made up of 78.1 per cent nitrogen, 20.9 per cent oxygen, and 0.9 per cent argon, with 0.03 per cent carbon dioxide, and traces of other gases. It usually contains, in addition to these gaseous elements, a certain amount of finely divided solid matter in the form of dust particles. Analyses made under my direction during the past summer have shown this dust to be present to the amount of something less than one-tenth gram per million liters of air, or 5,000 dust particles per liter, in the air of New York City on a clear day. At the other extreme we found 22.2 grams per million liters, or 250,000 dust particles per liter, in a mattress factory, and still larger weights in a

starch factory. Bacteria are present in ordinary air to the number of 1 to 4 per liter—in very small numbers as a rule.

Five different changes take place in this normal atmosphere when human beings occupy a confined space.

1. The oxygen is reduced by respiration. Tigerstedt estimates the amount of oxygen absorbed by a man of average weight at rest as 764 grams, or 534 liters per 24 hours.

2. The carbon dioxide is increased by the same process. The oxygen consumption cited above with a respiratory quotient of 0.80 would equal 840 grams, or 427 liters per 24 hours.

3. There is given off into the air a greater or less amount of organic matter, which is perceived by us as odors—material given off not from the lungs to any extent but from the mouth, from the teeth, skin, and clothing.

4. The temperature of the air is raised by the heat given off in the process of metabolism. The number of calories produced in 24 hours corresponding to the oxygen consumption of 534 liters cited above would be 2,563.2 calories. About four-fifths of this, say 2,000 calories, is given off from the skin. Lusk and his associates have recently shown that the heat production bears a direct and close relation to the superficial area of the body and amounts for a resting individual to 953 calories in 24 hours per square meter of body surface (corresponding to an oxygen consumption of 198 liters per square meter of body surface).

5. The humidity of the air is increased by the moisture given off in the breath and from the skin. The amount of moisture evaporated has been estimated as in the neighborhood of 1,400 grams in 24 hours for a man at rest. All of these values may be greatly increased by active exertion, and the amount of water given off in particular is radically altered by the heat and humidity of the surrounding atmosphere.

In seeking among these various changes for the cause of the physiological effects of vitiated air it was perhaps natural that the mind should turn to lack of oxygen as of prime importance. When a mouse is confined under a bell jar, it dies from oxygen starvation, and it was at first assumed that the same thing happens to a less degree in a badly ventilated room. As a matter of fact men do sometimes die from lack of oxygen in clogged sewer manholes (although poisoning by carbon monoxide is often at fault in such cases) or in the low parts of mines.

In such rooms as are ordinarily used for human occupancy, however, the changes in oxygen and carbon dioxide, even with the worst ventilation, are found to be comparatively slight. The oxygen may fall from 21 per cent to 20 per cent, and the carbon dioxide may rise from 0.03 to one-half per cent; greater changes than this are not observed even in the most crowded and worst ventilated room on account of the leakage through walls and ceiling and cracks of all sorts. These values are very far from the values which are found to produce harmful physiological effects. In mines the oxygen is often deliberately kept down to 17 per cent or less in the hope of avoiding the dust explosions that are likely to follow in freely ventilated mines during cold weather.

Some of the most interesting work along this line has been that in regard to the phenomena of mountain sickness. My colleague, Prof. Henderson, with the English physiologists Douglas and Haldane, made a most important series of studies of this kind on Pikes Peak two or three years ago. On Pikes Peak the partial pressure of oxygen present corresponds to about 13 per cent at ordinary atmospheric pressure. Under these conditions there are distinct symptoms of mountain sickness, blueness of lips and face, loss of appetite, nausea and vomiting, intestinal disturbances, headache, fainting, periodic breathing, and great difficulty in getting breath on exertion. But even here, with only 13 per cent of oxygen, after a few days the symptoms began to lessen, and after a few weeks of acclimatization the extreme conditions disappeared, although periodic breathing was still occasionally observed, and lips became blue on vigorous exertion. The investigators found that at least three things had happened

in this adaptation. In the first place the cells lining the alveoli of the lungs had acquired the power of secreting oxygen one way and carbon dioxide the other more vigorously for the same gaseous pressure than they would under ordinary conditions. In the second place the alkalinity of the blood had changed so as to stimulate the respiratory center with a less amonnt of carbon dioxide. And finally the hemoglobin had increased so as to supply the tissues more readily with the needed oxygen.

Many people live active and vigorous lives under such conditions as this. In the great city of Potosi, in the Andes, for instance, the partial pressure of oxygen is very close to that at Pikes Peak, and many famous health resorts at an altitude of 5,000 feet have a lower partial pressure of oxygen than obtains in the most crowded room.

Much the same thing is true in respect to carbon dioxide. Carbon dioxide may reach one-half per cent in badly ventilated rooms. In certain parts of many breweries it is maintained between one-half and 2 per cent without serious effects. The only result of a concentration of 2 per cent of carbon dioxide is an automatic 50 per cent increase in depth of breathing such as occurs with moderate exercise. Only when such an excess of carbonic dioxide is combined with vigorous exercise is discomfort experienced. By observations on conditions in various industries, and at various altitudes, and by detailed physiological experiments of many observers, it has been shown quite conclusively that oxygen may fall as low as at least 17 per cent and carbon dioxide may rise as high as 1 per cent without harmful physiological effects.

We must therefore turn to some other cause than changes in carbon dioxide and oxygen to account for the sensation of discomfort in badly ventilated rooms. This fact has been recognized for many years. Von Pettenkofer in the sixties worked the problem out broadly, although without the detail which is now available. Hygienists turned next to the organic matter, a subject much harder to study. It was simple to try out various percentages of carbon dioxide and oxygen, but with organic matter of a hypothetical nature the opportunity for mystic imaginings was much greater.

The conception of subtle organic poisons in the air is probably due to Brown-Séquard more than to any one else—Brown-Séquard, notable among biologists because he had three or four entirely erroneous opinions on important points which he supported by brilliant and apparently convincing experiments, and which it took decades to disprove. He believed that he could demonstrate the presence of organic poisons by condensing the material from the breath of animals and injecting it into other animals, which died as a result. It was later shown that they would have died in exactly the same way if the same amount of pure water at the same temperature had been injected. Then he placed animals in jars and allowed them to breathe the air breathed by other animals, once more with fatal results. These experiments were harder to control, but it was finally shown that the animals died from excessive carbon dioxide or from the chilling effect of excessive moisture. Many others have repeated these experiments excluding such factors, and all of them have obtained uniformly negative results.

The series of investigations conducted by Prof. Rosenau, of Harvard, about five years ago approached this question in a somewhat different way. If a minute amount of some foreign protein substance is injected into an animal, after a certain time the animal will become highly sensitive to that particular protein and will die in a few minutes from a second injection, with characteristic symptoms. This anaphylactic reaction is a test for the specificity of proteins. Rosenau attempted to use this method for the detection of very minute quantities of organic substances, and he believed that he had demonstrated that there were such substances present in the expired air. He collected, for example, the matter expired in the breath of a dog and injected it into a guinea pig, and later injected dog-blood serum into the guinea pig, when, as he believed, the guinea pig died with symptoms of anaphylactic shock, which would indicate that there was a specific protein substance given off in the breath, although of course not necessarily an intrinsically poisonous one. These experiments have now,

however, been repeated by three other observers, by Leonard Hill in England and by Weismann and Lucas in New York City, the latter of whom worked under my direction. All three entirely failed to confirm Rosenau's experiments.

There has been one series of investigations carried out during the past year by the New York State Commission on Ventilation, which again reopens this question in a different form. We have been carrying on rather extensive experiments for the past three years, to which I shall refer in more detail later on, in which human subjects were exposed to known air conditions and a wide variety of physiological and psychological observations made upon them. In the course of these experiments we thought it would be interesting to see whether heat had any effect on appetite for food. We served our subjects in the experimental chamber with a standard luncheon, and we weighed the amount that they left on the plates afterwards so as to see how much they had eaten. We did not find very striking results due to the heat, but we found what we had not expected, a marked effect of vitiated air as compared with fresh air at the same temperature. We gave our subjects on certain days fresh outside pure air at low temperature; on other days fresh pure outside air raised to a high temperature; on other days we kept the same air in the room all day, allowing it to become chemically vitiated, but regulating its temperature. We found to our great surprise that comparing the fresh air and vitiated air days with the same temperature and humidity there was a distinct difference in the amount of food eaten. One series of experiments showed more food eaten on the stale air days, 4.9 per cent more for the whole squad of subjects; but this series had been stopped in the middle before calculating the results, because the religious prejudices of the subjects had entirely destroyed its value. We happened to come across a series of fast days, and these subjects were women who were very orthodox, and we found that ritual was governing the amount they ate, not air condition. The other four series which were completed show uniformly an excess of food eaten on fresh-air days, the excesses in the four series amounting to 4.4, 6.8, 8.6, and 13.6 per cent, respectively. There were from 71 to 160 meals served in each series, and we believe the results to be significant. We have tried to produce the same effect with fresh air containing carbon dioxide, without success. We have tried it with air containing artificial odors, without success. My personal hypothesis is that there is a psychological effect or reflex reaction to the body odor which had that subtle effect on the appetite. At any rate it stands as the one demonstrated effect of the chemical constituents of normally vitiated air.

It was, I think, Hermann who in 1883 first pointed out that heat and moisture were probably the factors that produced the bad effects of bad air rather than its chemical composition, but most of the fundamental work on the subject was doné in 1905 or thereabouts by Flügge and his pupils. These experiments have been repeated by Hill and Haldane in England, and by Benedict and others in this country, and all of the results have tended to show that Hermann was correct, and that the people in the Black Hole of Calcutta died, not of oxygen starvation, but of heat stroke.

In these experiments the subjects when placed in carefully controlled closed chambers experienced the symptoms that one is accustomed to associate with badly ventilated rooms. If the subjects in these rooms were allowed to breathe outside air through a tube they were not relieved. If subjects outside were allowed to breathe the vitiated air through a tube, they did not experience discomfort. These two simple experiments appear to be entirely conclusive as to subjective symptoms. The feeling of uncomfortableness affected the men in the chamber, not the men outside the chamber, whatever air each group was breathing. It was the heat and moisture produced by their bodies which caused the feeling of discomfort, by its effect not on the lungs but on the skin. Benedict showed that a man could live for many days in a closed chamber without damage to his health and without having any idea that anything was wrong, with 1 to 2 per cent of carbon dioxide present, provided the chamber was cool and dry.

Leonard Hill comments on his experiments in England as follows:

In one class of experiments we shut within the chamber seven or eight students for about half an hour and observed the effect of the confined atmosphere upon them. We kept them therein until the CO_2 reached 3 to 4 per cent, and the oxygen had fallen to from 17 to 16 per cent. The wet-bulb temperature rose meanwhile to about 80° to 85° F. and the dry bulb a degree or two higher. The students went in chatting and laughing, and by and by as the temperature rose they ceased to talk and their faces became flushed and moist. We have watched them trying to light a cigarette (to relieve the monotony of the experiment) and puzzled by their matches going out, borrowing others, only in vain. They had not sensed the percentage of the diminution of oxygen, which fell below 17. Their breathing was slightly deepened by the high percentage of CO_2, but no headache occurred in any of them from the short exposure to from 3 to 4 per cent CO_2. Their discomfort was relieved to an astonishing extent by putting on the electric fans placed in the roof. Whilst the air was kept stirred the students were not affected by the oppressive atmosphere. They begged for the fans to be put on when they were cut off. The same old stale air containing 3 to 4 per cent CO_2 and 16 to 17 per cent O_2 was whirled, but the movement of the air gave complete relief, because the air was 80° to 85° F. (wet bulb), while the air enmeshed in their clothes in contact with their skin was 98° to 99° F. (wet bulb). The whirling away of this stationary air cooled the body effectually, for air at 80° to 85° F. holds considerably more water vapor when heated up to from 98° to 99° F.

In our experimental plant in New York we have been repeating these experiments in somewhat more detail as regards the special physiological reactions involved. Our observation room is 10 by 14 by 10 feet high, very carefully insulated as to walls and ceiling, entered by passages through three doors, and arranged so that we can control with a high degree of accuracy the temperature and humidity and air flow. We have placed in that chamber from four to eight subjects at a time, each squad of men or women being observed from four to eight hours a day for a period of two to eight weeks. We found that chemically vitiated air of a comfortable temperature and humidity had no effects on any physiological or psychological reaction except on appetite. High temperature (86° with 80 per cent relative humidity) produced a slight but distinct elevation of the body temperature, an increase in reclining heart rate, an increase in the excess of standing over reclining heart rate, a very slight lowering of systolic blood pressure, and a marked fall in the Crampton value (a ratio between the change in heart rate and the change in blood pressure on passing from a reclining to a standing position). Broadly speaking a high Crampton value means that the vaso-motor system of the body adjusts itself easily to the work of standing up after lying down.

Moderately high room temperature (75° with 50 per cent relative humidity) had the same effects, although of course in less degree. Even the extreme room temperature of 86° with 80 per cent relative humidity combined with high carbon dioxide showed no effect on the respiratory rate, dead space in the lungs, chemical composition of the blood, or the rate of heat production or digestion or metabolism or any other physiological reaction studied.

We next went on to the question of the study of efficiency—the ability and desire to do mental and physical work. We found that even a temperature of 86° produced no effect on the power to do mental or physical work. When subjects were working under pressure, accomplishing all they could in a brief period of time, they did just as well under bad conditions as under good conditions. We ought not to be surprised at this. It is our own experience; on a hot day in summer we play tennis or do a piece of absorbing intellectual work just as well as in colder weather.

We had therefore to adopt other methods. Prof. Thorndike, of Columbia, devised tests in which the subjects were allowed to work or not work as they chose, and were paid a small amount if they accomplished a certain quota of work, giving a slight but only a slight incentive, imitating the condition that exists in schools and in factories that are not on piecework.

We obtained marked and striking differences from these option tests. The amount of physical work done when the subject had the choice of working or not dropped

15 per cent at the 75° temperature as compared with the 68°, and dropped 37 per cent at 86° as compared with 68°.

We found no such effect on the optional tests for purely mental work. On the contrary we found that the amount of mental multiplication done optionally was 4.9 per cent more at 75° than at 68°. I am inclined to think that this was perhaps due to the stimulus of the slight discomfort, and a desire to keep the mind off the outside conditions by working. As soon as we got to typewriting, involving again a modicum of physical work, 6.3 per cent more was done at 68° than at 75°. I think these experiments show that overheating has a serious and important effect on the actual output under normal working conditions. The results should be significant for the school trustee, and for the office manager and factory manager. They show definitely what has been generally assumed without any quantitative basis of proof, that there is a large loss in efficiency due to overheating.

Prof. Ellsworth Huntington, of Yale University, carried out a year or two ago some extremely interesting experiments along this line on the effect of season upon mental and physical work—physical work of operatives in Bridgeport and mental work of students at West Point and Annapolis. He showed that there was a distinct falling off in the amount of work when the outdoor temperatures went above 65° or 70°. He found that there was a still more marked decrease when the temperature fell below 40° to 50°. There was thus a period of maximum productivity in both factories and educational institutions in spring and fall, with a minimum period in winter and another minimum in summer. Sudden changes, on the other hand, in either direction were stimulating. In Prof. Huntington's book on Civilization and Climate he connects these observations in a most interesting and suggestive way with the efficiency of mankind under the various climates of the globe.

A word should be said as to one other important effect of excessive temperature, its influence upon infant mortality. It might be supposed that the infant, having more surface to get rid of the heat in comparison with its bulk, would not suffer severely from heat, but this advantage is much more than overbalanced by the greater sensitiveness of its organization. The combined effect of artificial feeding and high atmospheric temperature is what causes the great loss of infant life from summer complaint. A young baby can usually live in cold weather even when fed with cow's milk; a baby can live through severe summer weather if it is fed at the breast. The combination is the deadly thing.

Investigations in Berlin and elsewhere have shown that the infant mortality in summer is of two distinct types. In the first place, during early summer there are deaths among infants due to direct heat stroke, sudden short illnesses due, primarily to the effect of heat, but occurring almost exclusively among infants artificially fed. Later the babies die from summer complaint, from long drawn out diarrhea, in which the milk plays a somewhat larger part, but in which the lowering of the vital resistance by heat is an integral factor.

I look forward to the day when there will be not only artificially cooled hospital rooms for babies, but cool day and night nurseries in the crowded tenement districts where babies can be taken when a severe spell of weather sets in. There is very little question that such a provision is quite as important, if not more important, than the provision of warm habitations in winter.

Finally, one other effect remains to be considered—the effect of atmospheric conditions on the membranes of the nose and throat. Benjamin Franklin said "that people who live in the forest, in open barns, or with open windows, do not catch cold, and that the disease called 'a cold' is generally caused by impure air, lack of exercise, or from overeating." This general phenomenon is of course very familiar; yet there has been little exact scientific evidence on this point. This is a subject which the New York State Commission on Ventilation has been taking up during the past year in a series of experiments under the immediate direction of Dr. James Alexander

Miller. With our experimental rooms we were able not only to expose the subject first to a hot condition and then to a cold condition, and vice versa, but by having them bend over in a somewhat uncomfortable position we could have the body in one room exposed to one atmosphere, and the head in another exposed to another atmosphere.

These experiments confirmed the conclusions of Hill and Muecke that in going from a hot room to a cold room the membranes of the nose become paler and less moist, while the inferior turbinates contract.

We found, however, that when the change was too sharp, when the subject passed from a hot room into a cold room with a strong draft on the face, it frequently happened that while the redness of the membranes decreased, the swelling and paleness did not decrease but often increased, so that the membranes were swollen and bathed with mucous secretion, but without an ample blood supply—an ideal condition for the cultivation of disease bacteria. Apparently this is the phenomenon which lies at the base of "catching cold" by going from a hot room into the cold air.

We examined a number of workers who had lived under abnormal conditions—furnace men, exposed to hot dry air; laundrymen, exposed to hot, moist air; and truckmen and teamsters, exposed to severe outdoor-air conditions. We found abnormal reactions among these subjects in much greater degree; and these occupational groups showed much more chronic nasal disease than did the student subjects. About 3 per cent of the students had chronic diseases of the nasal passages, 19 per cent of the outdoor workers, 35 per cent of the furnace men, and 46 per cent of the laundrymen. Both the experimental work and this statistical work on the various occupational groups pointed to the very serious effects of hot, dry air upon the mucous membranes, and particularly the danger of passing from such a condition into chill outdoor air.

These are the things we know, or think we know, about air. We hear a great deal about other subtle and mysterious effects, about "canned air," and the bad effects of bringing in air through ventilating ducts instead of through windows. I have never had any great sympathy with this phrase or with the idea that anything harmful necessarily happened to air because it went through galvanized-iron ducts instead of coming through a window frame. Its temperature and humidity may be altered. Those are things which we know about and can measure. Whether there is any other factor at work, I do not know. Our own observers on the commission staff are constantly reporting to us that window-ventilated rooms seem fresher than those ventilated by mechanical-ventilating systems. I suspect, however, that these differences, when more carefully analyzed, will be found to be due either to odors or to variations in temperature or humidity or to the factor of air movement.

Air movement is one of the most important elements in the problem, since it largely controls the temperature and moisture effects upon the human body. The body is surrounded, as Prof. Sedgwick has expressed it, by an "aerial blanket" of hot, moist air. Wind breaks up this hot, moist envelope and drives it away, reducing the temperature of the body to that of the surrounding air. Leonard Hill has given us a useful instrument for measuring these effects. This apparatus consists simply of two thermometers graduated from 86° to 110°, one a dry bulb, the other an ordinary wet bulb, which is chilled by the evaporation from a cloth surrounding it. These thermometers are first heated until they rise to about 110°, and the time taken to fall from 100° to 90° is noted. This measures the combined effect of three factors, the temperature of the outside air, the humidity of the outside air, and the air movement; and it measures these three factors very much as they affect our own body. I have been making observations with this instrument during the past summer. The limits of comfort set by Prof. Hill, and which I think are reasonably near the truth, are three minutes for the fall of the dry bulb and one minute for the wet bulb. In one of my observations in a room before a fire when the temperature was 72°, the dry bulb took 4 minutes 37 seconds to fall; the wet bulb 1 minute 18 seconds. On another day

outside in a wind the thermometer was at 82°, yet it took only 3 minutes for the dry bulb to fall and 42 seconds for the wet bulb. This is why we feel so much more comfortable out of doors in summer, with a high temperature, when there is a good wind, than we do in a closed room when the temperature gets a very little over 70°.

On one exceedingly uncomfortable day in September in my laboratory in New York at a temperature of 79° it took 5 minutes 55 seconds for the dry bulb to fall, and 1 minute 35 seconds for the wet. We turned on the electric fan, and it took 1 minute 58 seconds for the dry bulb to fall and 29 seconds for the wet bulb. This instrument gives at last an opportunity of measuring the effect of air movement, which is probably one of the most important things in determining our comfort.

Prof. Henderson has urged, in view of the similarity between the symptoms of mountain sickness and those produced by bad ventilation, that the temperature of the air may produce a hitherto unrecognized change in respiratory activity. The phenomena observed have however to do primarily, not with the lungs but with the vaso-motor system, which regulates the temperature of the body. Our bodies maintain their constant temperature of 98.6° at the poles and at the Equator by an exceedingly delicate system of adjustments, which leads to the dilation of the blood vessels in the skin when the air is hot and their contraction when it is cold. Moderately excessive heat causes the expansion of the skin blood vessels and robs the brain and internal organs of blood. I suspect that the disinclination to do physical and mental work is largely due to deficient blood supply in the brain. Under a stimulus we may overcome this, but ordinarily when the blood is in the skin we are sleepy and dull, and in extreme cases toxic effects result, when the mechanism of the body is seriously deranged by the heat, as in the Black Hole of Calcutta and in the case of heat stroke of infants in summer.

Extreme cold on the other hand also reduces efficiency as shown by Prof. Huntington. It lowers the vitality and may form an important contributing factor in respiratory and other diseases.

Moderate cold exerts a tonic effect, training the blood vessels of the vaso-motor system so that they will respond promptly to external changes. This system needs to be exercised just as any other system of the body does, and the question of ventilation is tied up with the problems of clothing and of bathing. The judicious airing and clothing and bathing of the body so that the vaso-motor system may be protected from extremes but educated so that it will meet moderate changes of temperature, with success—these are among the most important tasks of personal hygiene.

If the conclusions drawn by Prof. Ellsworth Huntington in his striking book are confirmed by future study, countries whose natural climates do not conform to the ideal he has worked out may find it possible to produce and maintain on an extensive scale those artificial conditions of coolness and changeableness which he finds necessary to stimulate the highest human efficiency.

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Dr. KOBER. I wish to express my appreciation of the very scientific work presented by Dr. Winslow and to utter a word of caution against drawing practical deductions which might perhaps lead to harmful effects. I am a thorough believer in pure air such as nature provides in the average composition of the atmosphere. It is stated that in the question of ventilation, the temperature, movement, and amount of humidity in the air play the most important part. While this is true, I believe there are decided differences in the purity of the air of our habitations and workshops when compared with out-door air, especially in air of parks, seashore, mountains and in the open country. I think it can be shown that differences exist not only in the amount of carbon-dioxide and oxygen, but also in the organic and inorganic constituents, as demonstrated by the presence of dust and bacteria, which always go hand in hand. So, for example, Uffelmann found that while the outer air contained only 250 germs per cubic meter, the air of his library contained 2,900, of his sitting room 7,500, of his bedroom 12,500, and the air of a living room of a workingman's family as many as 31,000 germs. He also demonstrated that they increased after disturbing the dust of the rooms with feather dusters or by slamming the doors, showing that they actually cling to the dust. It does not follow that because laboratory experiments failed to demonstrate any bad effects from the presence of large volumes of carbon-dioxide and a corresponding deficiency of oxygen, habitual exposure to vitiated air is harmless. It is far better perhaps to assume that every particle of impurities over and above the amount normally present, must of necessity influence the physico-chemical changes in respiration and, if continued for any length of time, health will be impaired. This belief is also in harmony with nature's beautiful process in storing up the excess of carbon-dioxide in the form of carbon in growing vegetation.

It will be difficult to account for the undue prevalence of tuberculosis among the North-American Indians except on the grounds that the change from the tepee with its copious ventilation, to bad housing conditions with insufficient ventilation has established a peculiar predisposition to the disease. It is the experience of the old practitioners of the Southern States that during the days of slavery the Negro on the plantations enjoyed as good health as the average white people

among whom they dwelt and that consumption was very uncommon among them. After their liberation these people had to find shelter as best they could in shacks and shanties wholly unfit for human habitations. Their tuberculosis rate was almost treble that of the white population in the city of Washington. This rate, which was 690 per 100,000 of the colored population in 1878, has been reduced to 359 in 1914.

When we condemned the buildings unfit for human habitations, they responded promptly to improved environments. Even live-stock shows the baneful effects of impure air, for tuberculosis among the range cattle of the far west, which are practically without shelter, is comparatively rare, while it affects from 15 to 25 per cent of the dairy herds, which are housed but without sufficient regard to light and air. As a matter of fact, an abundance of pure air has been found a most important factor in the prevention and treatment of tuberculosis, because it promotes the oxygenation of the blood, stimulates the appetite and nutrition and thereby increases the general resisting power of the system.

Improved ventilation and increased air space have lessened everywhere the death-rate, and it is chiefly by just such measures that the rate from consumption has been reduced, according to Sir Thomas Oliver from 7.82 to 2.5 per 1,000 in the British Army during the last 50 years. The tuberculosis and pneumonia death rate in the United States Army has been reduced respectively from 0.95 and 0.48 in 1901 to 0.49 and 0.28 in 1913, and similar gratifying reductions have been recorded in the United States Navy. It is to be presumed that then as now the recruits were selected with great care, and that the difference is simply due to the fact that they were subjected to impure air, incident to limited air space and have responded to improved environments.

The influence of overcrowding and bad air on diseases of the respiratory organs, amounting at times to epidemics, was well illustrated on the Isthmus of Panama. By scattering the colored laborers from crowded dormitories into single huts or rooms with not less than 50 feet of floor space for each individual, Gen. Gorgas reduced the pneumonia rate in a single year from 18.4 per 1,000 to 2 per 1,000.

It is also well known that pneumonia is more prevalent among the cavalry troops than among other arms of the service. Cavalry barracks have always the characteristic odor of horses and stables about them and it is not improbable that apart from exposure to the inhalation of dust during the grooming process, a part of this dust is also carried to the quarters and contaminates the air.

Personally I do not believe that the dangers of habitual exposure to impure air have ever been exaggerated and in my judgment no two factors have contributed so much to the reduction in mortality rates

during the last 50 years than the improvement of the air we breathe and the water we drink.

Lieut. Col. MUNSON. I want to thank Prof. Winslow for the extremely interesting paper he has given us. The subject, it seems to me, is one that has a side issue as well as a direct bearing on ventilation. I mean a climatological relation. To those who have been in the Tropics and in the Philippines there has lately come up the question of how long men should serve in the Tropics, and it has been decided by the War Department that probably two years would be sufficient. The question was considered pro and con as to whether physical deterioration did, or did not, occur among troops in a period less than that time. We know from the experiments which have been quoted to us here that a temperature such as we have in Manila means approximately a one-third decrease in the physical efficiency of people.

We know that just for a summer day or a week or two of hot weather we can force ourselves to work, but there comes a time when the constant pressure of unfavorable environment tends to reduce our will power to a point where we do not work at the same degree of efficiency. It has always seemed to me that possibly the sluggishness of the native, his unwillingness to work, which we looked upon with some contempt, was possibly due to the fact that he was more fit to live in that environment than the white man. The longer that we lived there, the less we wished to do, the less physical effort we wished to make, mental or physical effort. At the outset, we could make this mental effort fairly easily, but there came a time when this was reduced, and we had what the Army knows as "Philippinitis," a mental apathy and a physical sluggishness.

In these experiments of Prof. Winslow, in which he speaks of the psychological effect, I would rather be inclined to throw out the question of incentive, because the incentive is not the same to all. A dollar looks larger to one person than to another. One person will work harder for money than another. But the point is this, that no one willingly went along and did physical work. I should like to see what would happen if such experiments as Prof. Winslow's were continued not for days or weeks, but for months, until one got what we find in the Tropics, a physical inertia, gradual, slow in coming, but ultimately arriving.

In regard to indoor ventilation, one point seems to me to need emphasis. That is the point of proper humidifying of warm air. You will never find that worked out in anything but the most elaborately ventilated buildings. In Prof. Winslow's own town, which is my home, the people have no conception of it, and they overheat the houses at the same time they batten down the windows, preparatory to their annual six months' struggle with winter.

Dr. GUITERAS. I would like to say a few words in connection with the influence of heat, especially upon mental work. I am not convinced by these experiments. I have lived one-half of my life in a cold country and one-half of my life in a hot country, and I believe that as far as mental work is concerned, if you are entirely free from the prejudice that high temperatures make work impossible, you can do as much work in a hot climate as you can in a cold country. I think we forget what has been done in the past, how great civilizations in the past reached their height in hot climates. Even the people born in cold countries, when they have been brought into the tropical zone, have been able to do most extraordinary work. I do not think that anything the Spaniards have done, for instance, in their own country or throughout Europe could equal the amount of work and energy displayed both physically and mentally in the conquest of the Tropics in America. I think that there is a great deal of prejudice in education that makes us feel that we can not do work when a certain degree of temperature is arrived at. I have always maintained this and I have felt that I could do as much work in the Tropics as I could in a cold country.

Prof. SEDGWICK. It is not many years since we were all taught that the proper study in ventilation was the question of space. We must have so many cubic feet per capita, and it was figured out to be something like 400 cubic feet per capita. I have for some time referred in my classes to that as the per capita of fallacy, and the fact that Prof. Winslow has omitted all reference to it shows how dead it really is. Yet, if you pick up many books devoted to air and ventilation, you will find these figures still used, i. e., that all you need to obtain good ventilation is 400 feet or 500 feet per capita. I always illustrate the fallacy of that to my students by saying that I would rather have my head inclosed in a box of 1 cubic foot per capita with a good breeze going through the box than to sit in the biggest room in the world where there was no motion of the air at all; that is, I would rather have 1 cubic foot per capita of good, fresh circulating air than any number of feet per capita of stagnant air. Prof. Winslow has rightly concluded, I believe, that the large part of this question is the question of stagnation—stagnant air.

The CHAIRMAN. If there are no further remarks I will call upon Dr. Winslow to close the discussion.

Dr. WINSLOW. There are a few things I wish to take up. In the first place, Dr. Guiteras, as far as our experiments went, we found no diminution in the mental work, but rather the reverse. We found more mental activity as the temperature rose above 76°. We found a decrease in optional physical work, but an increase in optional mental work.

I may say with regard to the point raised by another speaker that we had of course our subjects under the same conditions, so that I think conditions were fair, but we did not, of course, work them for long periods of time. Now Prof. Huntington's work on students at West Point and Annapolis in classes in mathematics showed a diminution under high temperature, and these results show very strongly for a period of five years in the daily marks. Whether that is conclusive remains to be seen.

As to the question of dryness, I have always felt personally that very dry air was bad. Many people say dry air makes them nervous and that they feel badly. All I can say is that our work has failed to show any effect whatever on the membranes of the nose and throat. The most extensive experiments on the effect of dry air in nervousness, interfering with very delicate reactions have been made by Prof. Thorndyke. These results so far are negative. I think we must regard the bad effects of dry air *per se*, apart from heat, as unproved.

Col. HOFF. Prof. Sedgwick seemed to be inclined to question the effects of air space, cubic feet, etc. Are you proposing to eliminate that point entirely? Are we to adopt no standard of air space? In the Army we demand a minimum of 600 cubic feet and 60 square feet of floor space, and in our hospitals we require a larger allowance. Are we to eliminate that entirely? There is no doubt that movement of the air is an extremely desirable thing. For example, take the Caribbean Islands, where we have the trade winds the year through. I spent a couple of years in Porto Rico, and it did not seem to me that it was at all troublesome to do a great deal of hard work that had to be done down there at the time. On the other hand, in the Philippines, where wind is not blowing so constantly as it is in the Caribbean Sea, the situation seems to be somewhat different.

Dr. WINSLOW. I think it is probably true that there is a lower limit below which it is difficult to get motion of air without inconvenience. I am not sure that that 1-foot box really would be comfortable with the amount of air going through it, but I think what Prof. Sedgwick meant was that our present per capita standard was based on a wrong conception of our needs. The result of the British commission on factory ventilation was that there was no relation between the actual amount of air and the per capita space in the factory.

The CHAIRMAN. The following papers will be read by title before adjournment:

Climatologia dos Campos do Jordão S. Paulo, by Victor Godinho.

Nouveau procédé pour la transfusion du sang, par Louis Agote.

CLIMATOLOGIA—CAMPOS DO JORDÃO—S. PAULO.

Por VICTOR GODINHO,

Director do Hospital de Isolamento de São Paulo.

Ha dez annos que os Dres. Emilio Marcondes Ribas e Victor Godinho esforçam-se por obter dos poderes publicos do Estado de São Paulo e do Governo Federal do Brasil auxilios afim de construir sanatorios para tuberculosos e uma villa sanitaria para pessoas fracas, convalescentes, de repouso para os individuos enfraquecidos por qualquer causa, ou simplesmente veranistas.

Em 1908 conseguiram do Congresso do Estado a approvação de uma lei que lhes garantia uma subvenção annual de Rs. 60:000$000 durante 20 annos para construcção de sanatorios. Tratando então de estudar a climatologia das differentes localidades do Estado de São Paulo, reconheceram que a situação desejada estava situada nos Campos do Jordão a 1,640 metros de altitude, nas vizinhanças da villa Jaguaribe. É um lugar de clima privilegiado e gosando já de grande fama em todo o paiz, fama grangeada por innumeras curas alli conquistadas, desde longa data, por muitas centenas de tuberculosos.

É um clima de montanha, amenisado pela posição geographica, proxima da linha tropical, ao abrigo de ventos tempestuosos.

A villa Jaguaribe fica a 22° 44′ latitude sul e 45° 35′ de longitude a oeste de Greenwich. Pressão barometrica annual, 633.2 m. m., notando-se 164 dias por anno de dias claros. A temperatura media annual é de 13° 1′ (centigrado), sendo os extremos absolutos—7° e 28° 8′, havendo pois uma variação annual de 35° 8′. Nebulosidade media annual egual a 3.3 e humidade relativa variando de 61 a 95.

É pois um clima temperado situado em zona quente e modificado pela altitude e posição geographica. Quanto aos ventos temos uma taxa de 34 por cento de frequencia para as calmas, 27.4 por cento para os ventos seccos NE. e NW. e 16.7 por cento para os ventos humidos SW. e SE.

Convencidos que os sanatorios para tuberculosos deviam ser construidos nesse clima ideal dos Campos do Jordão, os dois medicos tiveram de reconhecer tambem que a viagem era extremamente incommoda para alli, precisando-se urgentemente construir uma estrada de ferro que ligasse Pindamonhangaba a villa Jaguaribe.

Por essa razão voltaram a solicitar ao Congresso Estadoal favores para a construcção para a referida estrada e por essa forma a concessão primitiva para construcção de sanatorios foi convertida em concessão para a Estrada de Ferro dos Campos do Jordão. Á sombra dos favores officiaes a estrada, que era o primeiro passo para conquista de um tão excellente clima e para a construcção posterior dos sanatorios, foi construida e vai ser encampada pelo Governo do Estado, visto os embaraços da companhia constructora em ultimar a obra. Só falta adquirir o material rodante e electrificar a tracção, o que o Governo fará. Por emquanto o trafego provisorio faz-se com machinas a vapor e automoveis de linha, apezar das rampas de 10 por cento na Serra da Mantiqueira.

A estrada começa em Pindamonhangaba, quasi a meio caminho entre Rio de Janeiro e São Paulo. A viagem na nova estrada offerece pontos de vista deslumbrantes, mais bellos do que o que se gosa na Serra do Mar atravessada pela São Paulo Railway. A altitude é muito maior, 1,750 metros acima do nivel do mar, no ponto mais alto da Serra da Mantiqueira, o horizonte muito mais vasto e os panoramas mais variados.

Campos do Jordão é uma região de campos naturaes em que são muito abundantes os pinheiros (*Araucaria brasiliensis*). Ha lá cerca de 2,000,000 de pinheiros de mais de 100 annos, prestando-se á exploração da madeira e sem despir os mattos. Todos os valles são cobertos de pinheiros, todos elles cercados de campos com excellentes pastagens para a creação de gado cavallar, bovino, ovino e suino. Estas creações

teem sido ensaidas com muito successo, mas são até agora pouco desenvolvidas por causa de difficuldade no transporte.

A villa Jaguaribe desde muitos annos é procurada por tuberculosos que na sua grande maioria lá encontraram a cura ou pelo menos uma melhora muito accentuada. No entanto, não ha ainda um sanatorio medelar e uma villa sanitaria, com todas as regras da hygiene, como projectam construir os dois facultativos.

Uma vez realisados esses projectos, a estação climaterica dos Campos do Jordão está destinada a attrahir concorrentes de todo o Brazil e mesmo dos paizes vizinhos, especialmente o Uruguay e a Argentina.

Os dois medicos fizeram contracto com a municipalidade de São Bento do Sapucahy para construirem na villa Jaguaribe 100 casas e gozam dos seguintes favores: isenção de impostos para as 100 primeiras casas; privilegio para abastecimiento de agua, luz e esgotos e para força electrica. A agua é abundante e purissima e as cachoeiras numerosas e de grande força. Uma dellas produz uma força de 12,000 cavallos.

A região presta-se admiravelmente para cultura das fructas: maçans, peras, pecegos, figos, etc. Muitas arvores fructiferas estão já plantadas e dellas se tem colhido fructos abuntantes e deliciosos.

Está em discussão no Congresso Federal um projecto concedendo garantia de juros de 6 por cento ao anno sobre o capital de Rs. 2,000:000$000 para construcção da villa sanitaria e sanatorios, isenção de impostos aduaneiros para o material de construcção e rouparia do sanatorio e das 100 primeiras casas.

Depende, porém, da resolução do Congresso. O escriptor desta pequena communicação tem esperança de dotar o Brasil de uma excellente estação climaterica, procurada como fonte de saúde, de repouso ou simplesmente de recreio, e junto da qual, na distancia de 6 kilometros, serão construidos sanatorios modelos para o tratamento dos tuberculosos. Elle é proprietario de 220 alqueires de terra, que adquiriu para os estabelecimentos que projecta, garantindo assim o começo de execuço do seu benemerito emprehendimento.

NOUVEAU PROCÉDÉ POUR LA TRANSFUSION DU SANG.

Par LOUIS AGOTE,

Professeur de Clinique Médicale, Buenos Ayres, Argentina.

La transfusion du sang, le recours précieux, au moyen duquel il est possible de sauver des milliers de personnes, victimes d'hémorragies intenses, n'a pu être utilisé pratiquement avec l'amplitude qu'on pouvait espérer de son indiscutable efficacité; ceci est dû, non seulement aux difficultés d'une manipulation compliquée et seulement réalisable par un chirurgien familiarisé en chirurgie vasculaire, mais aussi par les mortifications vraiment douloureuses souffertes par la personne donnant du sang. Nécessité de dénuer la veine dans l'espace suffisant afin de pouvoir faire la suture à la veine du malade, ce qui, en realité, constitue toute une opération chirurgicale. Ajoutez à tout cela, ce qui n'est pas dépréciable, le danger imminent des embolies dans le système circulatoire du malade, graves complications difficiles à éviter malgré toutes les précautions que l'on pourrait prendre. C'est ce à quoi l'on doit attribuer les cas de mort déjà observés. Comme si tout cela n'était pas suffisant pour restreindre l'emploi de la transfusion par l'anastomose artério-veineuse, il faut compter encore la circonstance aggravante de ne pas savoir exactement la quantité du sang transfusé; ceci peut ne pas avoir d'importance pour celui qui le reçoit, mais beaucoup

pour celui qui le donne (on a observé des cas de défaillance, syncopes, mort, etc.): le danger de l'infection des blessures produites afin de dénuer les veines, évité par des moyens parfaitement aseptiques—par exemple, dans une salle d'opérations—cela n'arrive pas ailleurs et spécialement dans les hôpitaux de campagne, en cas de guerre où la transfusion aurait un champ d'application vaste et efficace.

Tous ces inconvénients et d'autres que nous voulous taire afin de nous référer seulement aux plus forts, expérimentés dernièrement à l'occasion d'un essai de transfusion par les procédés recommandés spécialement par les chirugiens de l'Amérique du Nord, nous ont induit à étudier dans l'institut modèle de clinique médicale, l'intéressant problème afin de chercher sa solution partielle ou totale, profondément convaincus que la réaliser actuellement constitue un recours vraiment exceptionnel. Nos efforts réalisés en collaboration du docteur Ig. Imaz Appathie, médecin en chef des laboratoires de l'institut, ont donné des résultats favorables, permettant d'assurer que la transfusion du sang, c'est-à-dire l'injection de ce liquide provenant d'un sujet sain a un autre sujet malade, comme nous le conseillons, a perdu tous ces dangers, constituant un procedé clinique simple d'une exécution facile et à la portée de tous les médecins. *Il remplit alors les conditions exigées par la clinique médicale.*

Sans vouloir raconter l'histoire de nos travaux, essais, fracas et vacillations, jusqu'à l'arrivée à un résultat définitif et satisfaisant; sans vouloir discuter sur les diverses questions entrelacées à ce problème intéressant et qui sûrement se présenteront aussi à l'esprit du lecteur, il nous suffit d'assurer qu'elles ont été étudiées et résolues, soit par nos propres travaux soit par d'autres observateurs. Nous nous limiterons à la description de notre procédé, tel qu'il résulte de nos expériences concluantes, faites premièrement sur des animaux et ensuite sur des hommes, pouvant assurer sa parfaite innocuité.

Notre procédé est celui de la transfusion immédiate,[1] en prenant du sang de la veine du pli du coude du donnant, recueilli dans un récipient ou appareil dermoclyse, contenant une solution de citrate de neutre soude au 25%, dans la proportion d'un gramme pour cent grammes de sang. Ce mélange rend le sang incoagulable, sans qu'il perde ses qualités vitales. Comme le citrate neutre de soude est absolument inoffensif pour l'organisme en quantités beaucoup plus grandes, on peut injecter ce mélange au malade, avec toute facilité, sans aucun danger, dans les veines de l'avant-bras au moyen du même appareil et comme n'importe quelle autre injection endo-veineuse.

Cette merveilleuse propriété du sel de soude d'empêcher la coagulation du sang, fait de la transfusion une opération très simple, à la portée de tout le monde, supprimant définitivement les dangers présentés jusqu'ici, grâce à ce recours d'un effet très efficace. D'autre part, elle réduit l'acquisition du sang a la simple piqûre d'une aiguille en platine (le diamètre intérieur d'un millimètre est suffisant), suivant le même procédé de la saignée; personne ne verra d'inconvénients à donner une quantité déterminée de sang, sans s'exposer à souffrir, durant des jours, des conséquences comme nous le sommes de son innocuité; la transfusion sous cette forme doit entrer dans la pratique courante de l'assistance médicale, dans les cas indiqués et durant les époques de guerre comme actuellement elle constituera le recours suprême pour combattre les grandes pertes de sang.

On pourrait objecter à notre procédé l'emploi du sang veineux au lieu de l'artériel. Rappelons que l'emploi de l'anastomose artério-veineuse n'a pas été faite pour la qualité du sang, mais afin de pouvoir utiliser la forte pression artérielle, indispensable au moment d'une transfusion directe.

Libres par conséquent de cette imposition, nous pouvons utiliser sans danger le sang veineux, d'autant plus lorsqu'il appartient à la circulation périphérique, mais toute objection reste nulle, nous laissant libres d'utiliser la circonstance favorable de l'avoir à notre portée au moyen d'une simple piqûre.

[1] Nous avous fait la première transfusion le 14 de novembre de 1914.

Après tout cela, le liquide injecté, en pénétrant dans la circulation du malade va souffrir la même dépuration pulmonaire que celle à laquelle il a été soumis dans l'organisme du malade; il s'oxygène ainsi dans le récipient comme dans le poumon. L'observation aurait sa raison d'être s'il s'agissait de sang pris dans une veine . . . d'une viscère (du foie ou du rein).

MANIÈRE DE PROCÉDER.

L'opération n'offre aucune difficulté. On peut, à la rigueur, employer l'appareil de Potain ou n'importe quel autre semblable, utilisé pour les injections endo-veineuses. Nous conseillons l'emploi d'un modèle construit par la maison Lutz y Schulz de cette capitale, d'après nos indications. L'appareil se compose d'un récipient en verre gradué à deux tubes, avec ouverture relativement large. On cherche que le sang tombe directement de la canule au récipient dont le fond se termine en pointe, afin que le tube injecteur en verre arrive au niveau plus bas du liquide et permette ainsi d'utiliser, sans que l'air entre, la plus grande quantité de sang, circonstance très importante lorsqu'il s'agit de cette matière. La branche la plus longue porte l'aiguille en platine pour l'injection, unie au moyen d'un tube en caoutchouc, d'un calibre intérieur plus ou moins égal à celui du tube en verre, et la plus courte de laquelle de diamètre suffisant afin de pouvoir le tenir en position verticale.

Elu le donnant et qu'on est assuré de sa parfaite santé, en pratiquant toujours, si cela est possible, la réaction de Wassermann, refusant celui dont le résultat a été positif même quand il s'agit d'un malaise spécifique en se rappelant des diversités des *spiroquetes*, avec ses conséquences pour le pronostic. On prendra le sang dans la veine du donnant, sans couper la peau, au moyen de l'aiguille en platine, après avoir lié le bras plus haut que le pli du coude, ou en incisant la veine par une incision comme dans n'importe quelle saignée. On recueille le sang dans le récipient choisi dans lequel on déposera préalablement trois grammes de la solution nommée plus haut, quantité suffisante pour trois cents grammes de sang, même lorsqu'on n'arrive pas à recueillir la dite quantité, puisque étant inoffensif pour l'organisme, ce surplus n'a aucune importance. Il est convenable d'agiter doucement l'appareil pendant que l'on recueille le sang, afin de faciliter le mélange des deux liquides et d'éviter la coagulation dans les parties libres de son contact. Ceci fait, on l'injectera dans la veine du malade, suivant le procédé ordinaire pour les injections dans les veines, en prenant les précautions du cas.

L'extraction de 300 grammes de sang chez un individu normalement robuste est facilement tolérable.

Afin d'éviter une syncope ou une simple défaillance on peut lui faire préalablement une entéroclyse de 300 grammes de sérum. On peut ainsi injecter après avoir pratiqué l'extraction de la même quantité de la solution saline dans la veine donnant. L'absorption du sérum par le rectum est presque simultanée avec le sang, de manière que celui-là conserve en tout temps son équilibre circulatoire.

Après la transfusion on n'observe pas de température, ni rien de particulier. Nos affirmations ont été faites après avoir analysé soigneusement les urines recueillies de deux en deux heures, ce qui montre l'incorporation complète du sang injecté dans la masse sanguine du malade. Quant à l'examen du sang, celui-ci a démontré l'augmentation des éléments figurés et de l'hémoglobine, comme la tension sanguine et la réduction de la tachycardie. Consécutivement à ces signes l'état général du malade est mieux.

The CHAIRMAN. This completes the program of the afternoon, and the session is adjourned.

SESSION OF SUBSECTION B OF SECTION VIII.[1]

NEW EBBITT HOTEL,
Wednesday morning, January 5, 1916.

Chairman, SAM L. ROGERS.

GENERAL TOPIC:

Pan American Theme: Progress of Vital Statistics in Pan American Countries.

The session was called to order at 9 o'clock by the chairman.

UNIFORMACIÓN DE LAS ESTADÍSTICAS DEMOGRÁFICAS Y DE LA FECHA DE LEVANTAMIENTO DE LOS CENSOS DE POBLACIÓN DE LOS PAÍSES PANAMERICANOS.

Por ÁLVARO COVARRUBIAS ARLEGUI,
Jefe de Sección de la Oficina Central de Estadística, de Chile.

INTRODUCCIÓN.

En el presente trabajo no aparecerán cifras que den a conocer demográficamente los países panamericanos, ni trataremos de demostrar la necesidad de que cada uno de ellos organice la estadística del ramo; pues ya no se discute que este servicio forma parte integrante de la administración y que si alguno no cuenta aun con él, no es porque se desconozca su importancia, sino por causas de otro orden que no es del caso analizar.

Por lo tanto, el presente trabajo tiene por objeto proponer, en forma especial, la uniformación de las Estadísticas Demográficas para hacerlas comparables entre sí proponiendo a la vez, entre otras cosas, la reducción de las muchas materias que hoy comprende la demografía y que no están claramente determinadas.

PARTE I.—*Definición de la demografía.*

Etimológicamente la palabra demografía se deriva de la griega Demos, que significa pueblo y Graptein, describir; o sea, descripción de los pueblos.

Se puede decir que el creador de esta palabra fué el doctor en ciencias y sabio botánico, Aquiles Guillard, que la usó por primera vez en el Congreso de Bruselas el año de 1853, definiéndola de la siguiente manera: "Es la historia natural y social de la especie humana" y en un sentido más restringido: "Es el conocimiento matemático de las poblaciones, de sus movimientos generales, de su estado físico, civil, intelectual y moral."

Desde esa fecha, casi todos los escritores sobre estadística o ciencias sociales y las personas dedicadas a esta clase de estudios la han definido en sentidos diversos.

E. Lavasseur, en su libro sobre la población de Francia, la define: "Es la ciencia de la población: ella estudia sus movimientos y principalmente sus nacimientos, matrimonios, defunciones y su inmigración; ella se esfuerza por llegar a conocer las leyes que los rigen. Es la ciencia de la vida humana en su estado social."

[1] There was no stenographic report of this session.

Ferraris dice: "Es la ciencia de la población." Mesadaglia: "Es la ciencia estadística de la población," y Benini: "Es la ciencia cuantitativa de la población."

Estas definiciones y muchas otras han formado algunas sin autores conocidos, por ejemplo: "Es la ciencia del hombre considerado socialmente y en cuanto pueda ser expresada por medio de cifras numéricas"; otra: "Es el estudio y descripción de los pueblos, teniendo en cuenta la edad, profesión, domicilio, etc., de los individuos."

Las definiciones anteriores nos demuestran dos cosas: que existe disconformidad de apreciaciones y que, según las épocas, se restringen o ensanchan las materias que debe comprender la demografía.

PARTE II.—*Materias que comprendía la demografía.*

Por las definiciones anotadas se deduce que el campo de acción de la demografía es casi ilimitado; pues abarca la mayoría de las estadísticas que se relacionan con los hombres. Ella comprende la natalidad, nupcialidad, mortalidad, instrucción, justicia, criminalidad, migración, estadísticas morales, políticas, religiosas, etc.

Sin entrar a profundizar cada una de estas materias, se ve que, aunque ligadas indirectamente entre sí forman un bloque hetereogéneo de difícil amalgamación.

PARTE III.—*Segregación de algunas materias que comprendía la demografía.*

En un principio no presentó mayores dificultades el estudio de la demografía en la forma amplia en que fué concebida; pero el avance de las ciencias dió a conocer que algunas de las materias comprendidas en ella, debían ser investigadas independientemente, para lo cual se necesitaban informaciones distintas que para las demás.

Estas nuevas investigaciones trajeron como consecuencia la desmembración de la demografía, y lentamente los Institutos de estadísticas publicaron trabajos especiales sobre muchas de ellas, dejando para ser tratadas en conjunto sólo aquellas cuyas informaciones provenían de una misma fuente.

PARTE IV.—*Materias que debe comprender la demografía.*

Como se ve, en la desmembración de que hablamos no ha intervenido directamente institución o persona alguna, sólo ha sido originada por la fuerza de las circunstancias.

De aquí que en la actualidad no se sepa con exactitud las materias que legítimamente le corresponden; imponiéndose pues la necesidad de establecerlo de una manera categórica.

La práctica que en este caso ha representado la opinión de la mayoría de los demógrafos, ha fijado ya casi definitivamente las materias que debe comprender y que son: los matrimonios, nacimientos, nacidos-muertos y defunciones.

Existen también razones de otro orden que concuerdan con las fijadas por la práctica y que omitimos anotarlas aquí para hacerlo en el capítulo siguiente.

No contrariando lo establecido por la práctica ninguna disposición, falta para darle fuerza legal un acuerdo internacional.

Por tanto se entenderá en lo sucesivo por demografía la ciencia que trata exclusivamente de los nacimientos, matrimonios, nacidos-muertos, defunciones y sus derivados.

Como la palabra derivados encierra la mayoría de las informaciones, anotamos las que a nuestro juicio debe comprender: derivados de los matrimonios son los divorcios; de los nacidos-muertos, los fetos y abortos y de las defunciones, los suicidios.

Posiblemente causará extrañeza que la migración que está íntimamente ligada con el aumento de la población, haya sido eliminada de la demografía; pero para obrar de esta manera nos hemos apoyado en el siguiente argumento:

Cuando los medios de locomoción no habían alcanzado el desarrollo actual la migración, relativamente reducida, constituía sólo un hecho social secundario que podía ser tratado en conjunto con las demás materias demográficas. Pero actualmente las cosas han variado en absoluto y la migración constituye hoy día un problema de vital importancia para algunos países, pues de él depende en muchos casos, la prosperidad futura.

Por esta causa los países de migración intensa han separado las estadísticas migratorias de las demográficas, propiamente dichas, a fin de poder conocer a fondo los muchos problemas que ella encierra.

En consecuencia, creemos que la demografía no debe comprender la migración y que su programa debe ser sólo el que anotamos anteriormente.

PARTE V.—*Conveniencia de adoptar una definición de la demografía.*

A pesar de existir innumerables definiciones de la demografía sin embargo, la mayoría de los autores está de acuerdo en que no existe ninguna clara y precisa.

Recordando las muchas materias que encerraba se comprenderá fácilmente que las definiciones no fueran rigurosamente exactas y que no expresaran su verdadero significado.

Como lo hemos tratado de demostrar, el progreso de las ciencias en general y el avance de los estudios sociales en particular, ha hecho que la demografía no comprenda ya el gran número de materias que abarcaba en su origen.

De aquí que las definiciones existentes ademas de no ser concretas no expresen lo que es hoy la demografía. Por esta causa es necesario crear una definición que revele con exactitud su verdadero significado.

Estando ya los límites de ella perfectamente delineados no es difícil encontrar una definición concisa, clara y exacta y que concuerde con la etimología de la palabra.

Para esto hay que dejar establecido que los acontecimientos naturales más importantes de la humanidad son los nacimientos y las defunciones, puesto que constituyen el principio y el fin de la vida, y que todos los demás hechos están subordinados a ellos.

Hemos dicho que etimológicamente la palabra demografía significa descripción de los pueblos. Dejando establecido que los nacimientos y defunciones son sus acontecimientos más importantes, es natural que la descripción de ellos se refiera a estos acontecimientos principales y no a otros de menos importancia.

(El fondo de esta argumento lo hemos tomado también en consideración para dejar reducida la demografía a las cuatro materias anotadas en el capítulo anterior.)

De aquí que la definición de la demografía tomando en cuenta su etimología y las materias que comprende, sería: "descripción de los pueblos según sus principales acontecimientos naturales."

A esta definición hay que agregarle algo para que abarque la nupcialidad, que por no ser creación de la naturaleza, no es acontecimiento natural y por tanto está eliminado de ella.

Dada nuestra organización social, el matrimonio ha pasado a formar casi un acontecimiento natural (a pesar de haber sido creado por el hombre) pues, es el que legaliza la reproducción de la especie humana y el que constituye la familia, base del engrandecimiento de las naciones.

Por tanto, la definición anterior podría quedar en la siguiente forma: "Entiéndese por demografía la ciencia que trata de la descripción de los pueblos según sus principales acontecimientos naturales y legales, en cuanto a la nupcialidad se refiere."

PARTE VI.—*Uniformidad de las estadísticas demográficas panamericanas.*

Es un principio estadístico que todas las informaciones de una misma naturaleza, para que sean debidamente aprovechadas, deben ser uniformes.

Consecuente con este principio, casi todos los Congresos de estadísticas han tratado de uniformar las demografías a fin de hacerlas comparables entre sí. En este sentido se han aprobado diferentes acuerdos; pero pocos han sido los que se han llevado a la práctica en la forma estricta en que se han aprobado.

De estos acuerdo tal vez el adoptado por el mayor número de países panamericanos ha sido el de la nomenclatura internacional de causas de muerte, pero desgraciadamente no ha sido puesto en práctica en la forma exacta en que fué aprobado.

Revisando las publicaciones demográficas se vé que unos han adoptado sólo la nómina de causas de muerte; otros, la tabla de edades y por último, los hay, que han

adoptado ambas cosas, pero en forma tal, que con las edades no se pueden formar los grandes grupos de que trata la misma nomenclatura.

Por esta causa las estadísticas demográficas pan americanas no se prestan a estudios comparativos.

Esta dificultad para ceñirlas a un mismo plan se debe a defectos de los planes propuestos con este objeto y a la forma como han sido aprobados, según trataremos de demostrarlo.

El servicio de estadística demográfica ha sido organizado en cada país en conformidad al régimen administrativo y el sistema de investigación y publicación, en relación a los problemas que desean conocer. De aquí que cada uno tenga su sistema propio y diferente de los demás, según se comprueba por las respectivas publicaciones. Así, por ejemplo, mientras un país le da gran desarrollo a nupcialidad, el otro apenas la menciona y mientras éste usa la palabra varón y hembra para determinar los sexos, el otro emplea el de hombre o mujer o masculino y femenino, etc.

Luego, el fracaso de la uniformación de las estadísticas demográficas ha provenido de que los planes propuestos anulan los sistemas en uso, y como éstos han sido creados según las necesidades propias de cada país, los nuevos sistemas no les han reportado utilidad mayor.

En consecuencia, para llegar a conseguir que se uniformen las estadísticas demo gráficas de los países panamericanos es necesario que los acuerdos que en este sentido se aprueben no envuelvan, ni directa ni indirectamente, reforma alguna en las estadísticas existentes, ni tampoco anulen o hagan cambiar los procedimientos en uso.

Por tanto, para llegar a este resultado y obtener éxito en la práctica respecto a la uniformidad de ellas, proponemos la aprobación del siguiente acuerdo:

"Los países panamericanos formarán y publicarán sus estadísticas demográficas en la forma, fecha e idioma que lo estimen por conveniente; pero tendrán la obligación de hacer figurar en un capítulo o folleto especial, las informaciones demográficas en la forma e idioma acordado por el Congreso. Este capítulo o folleto se titulará "Informaciones demográficas acordadas por el Segundo Congreso Científico Panamericano."

Respecto al idioma creemos que siendo el español el de la mayoría de los países panamericanos deberá ser éste el que se adopte.

PARTE VII.—*Datos que Comprenderán las Informaciones Demográficas Panamericanas.*

Habiendo dejado establecido que la uniformación propuesta no se refiere en ningún caso a las estadísticas demográficas generales de cada país, sino a un capítulo especial de ellas, es necesario, por tanto, establecer con claridad los datos que el citado capítulo o folleto debe comprender y la forma como se publicarán.

Estos datos deberán ser de interés principal y general; pero, como para determinar ambas condiciones se necesitan conocer los problemas sociales, económicos, nosológicos, etc., de cada país; y, como esto sería materia de un trabajo largo y prolijo y que se prestaría a apreciaciones erróneas, nos concretaremos a anotar nominativamente los que a nuestro juicio pueden ser clasificados como de interés principal de cada país y general para todos, haciendo solo un ligero análisis de ellos e insertando al final los formularios respectivos.

Para obrar con orden anotaremos primero los datos que se refieren a los matrimonios, después los que se refieren a los nacimientos; en seguida los de nacidos-muertos y por último los de defunciones.

(A) MATRIMONIOS.

Número total de matrimonios y proporción por mil habitantes.

Número de matrimonios clasificados según el grado de parentesco de los contrayentes y detallados en urbanos y rurales. (Formulario No. 1.)

Número de matrimonios clasificados según la nacionalidad de los contrayentes y detallados en urbanos y rurales. (Formulario No. 2.)

(B) NACIMIENTOS.

Número total de nacimientos y proporción por mil habitantes.

Número de nacimientos clasificados según la legitimidad y el sexo y detallados en urbanos y rurales. (Formulario No. 3.)

Número de nacimientos clasificados segun la nacionalidad de los padres y la legitimidad y sexo de los nacidos, detallado en urbanos y rurales. (Formulario No. 4.)

Número de nacimientos clasificados según la clase de los partos, detallados en urbanos y rurales. (Formulario No. 5.)

(C) NACIDOS MUERTOS.

Se comprenderá en este rubro todos los que la nomenclatura internacional de causas de muerte clasifica como tales y además los abortos, fetos, etc.

Número de nacidos muertos clasificados según la legitimidad y el sexo, detallados en urbanos y rurales. (Formulario No. 6.)

(D) DEFUNCIONES.

Número de defunciones (descontados los nacidos muertos) y proporción por mil habitantes.

Número de defunciones clasificadas por causa, edad y sexo, detalladas en urbanas y rurales. (Formulario No. 7.)

Número de defunciones clasificadas según el estado civil y el sexo, detalladas en urbanas y rurales. (Formulario No. 8.)

Número de fallecidos menores de un año, clasificados por causa, edad y sexo, detallados en urbanos y rurales. (Formulario No. 9.)

Número de fallecidos menores de un año clasificados por causa y agrupados por meses. (Formulario No. 10.)

Número de fallecidos menores de un año clasificados por edades y agrupados por meses del año. (Formulario No. 11.)

Los datos que comprenderá el capítulo o folleto de estadística demográfica Panamericana, deberán separarse los que se refieren a la parte urbana de los de la parte rural. Por ejemplo, de los matrimonios se anotarán independientemente los celebrados en las ciudades de los celebrados en los campos, etc. Para determinar esta clasificación se emplearán las abreviaturas (U) Urbano y (R) Rural.

Esta separación obedece a la necesidad de conocer la forma como se desarrollan en los campos y en las ciudades los diferentes problemas sociales, nosológicos, etc., pues es sabido que mientras algunos acontecimientos son antiguos en las ciudades, en los campos no se conocen, o vice-versa.

Además, la vida demográfica de las ciudades tiene características especiales y que si las informaciones de éstas van unidas con las de los campos, falséanse mutuamente haciéndose imposible su estudio.

Respecto a la edad de los fallecidos, la comisión internacional encargada de la revisión de la Nomenclatura Nosológica Internacional reunida en París en julio de 1909, determinó que la clasificacion de las edades debía hacerse tan detallada como sea posible. Las razones que se dieron sobre el particular se encuentran en las actas de dicha comisión, por lo cual omitimos anotarlas aquí.

Por esto las edades de los fallecidos se anotarán sin formar grupos de años, sino los años continuando, esto es: Menores de un año, de un año, de dos años, etc., agrupando sólo los de cien años adelante.

Siendo los estudios nosológicos de capital importancia para la humanidad, estimo que se debe aportar a ellos el mayor número de informaciones posible y más, cuando se trata de países nuevos como los panamericanos que en este sentido tienen muchos puntos no resueltos y aun desconocidos.

Para reforzar nuestra opinión anotamos la del Dr. norteame ricano, Carlos V. Chapin. "El registro de las estadísticas vitales es la base firme sobre la cual debe descansar

toda la estructura de la ciencia sanitaria práctica, con el objeto de aprender las leyes de las enfermedades y buscar sus remedios. Se debe tener un conocimiento exacto del movimiento de la población y de las causas de muerte."

PARTE VIII.—*Uniformación de las fechas de los censos generales de población en los países panamericanos.*

Casi sin excepción todas las materias que forman la demografía tienen como base la población y sus deducciones van encaminadas a conocer antecedentes o a explicar fenómenos de la poolación misma. Por esto se encuentran íntimamente ligados entre sí el censo y la demografía y es lo que nos ha inducido a tratarlo en este trabajo.

Todo lo propuesto es relativamente fácil de llevar a la práctica, porque depende casi únicamente de los Consejos o de los Directores de Estadística.

No así lo relativo a la fecha de los censos que, por lo que a Chile se refiere, está reglamentado por una Ley de la República.

Analizando este asunto con algún detenimiento se llega a la conclusión que presenta dificultades que no aparecen a primera vista.

En primer lugar hay que tomar en consideración la parte económica de la operación, que, con sus trabajos preliminares, escrutinios y publicación demanda un desembolso pecuniario considerable.

Otro factor es la situación de normalidad que se escoge para efectuar el censo, procurándose que no haya ningún problema trascendental que agite la población. Cierto es que algunas veces se efectúa sin tomar en consideración ninguno de estos factores; pero solo por circunstancias especiales.

Ahora bien, suponiendo que el congreso aprobara la uniformación de las fechas de los censos, al llegar la época fijada, habría países cuyo estado financiero no les permitiría en ese momento, cumplir el compromiso; a otros o su situacion política o social les haría imposible la ejucución del trabajo, o habiendo levantado el censo poco tiempo antes de la fecha, llamémosla panamericana, no lo repetirían, y por último, Chile tendría el Congreso Nacional que prestarle su aprobación.

Por estas causas y otras que sería largo de numerar, la fijación uniforme de la fecha de los censos de población, presenta grandes dificultades.

Demostrados ya los principales inconvenientes que en la práctica se presentarían y estando penetrado de su utilidad, considero que es indispensable encontrar la forma de solucionarlos.

Como para esto se necesita estudiar cada uno de estos inconvenientes a fin de poderlos remediar, estimo que la manera de llegar a un resultado es que el Congreso apruebe por el momento sólo la idea de la uniformidad de la fecha de los censos, dejando el detalle o sea la forma concreta del asunto, a cargo de alguna institución especial, la Oficina de la Unión Panamericana por ejemplo, para que en el próximo congreso científico presente un proyecto con todos los antecedentes, incluso la opinión de los gobiernos, respecto a la uniformacion de la fecha de los censos y a las informaciones que debe contener.

Concretando la idea expresada en el párrafo anterior, el acuerdo sería el siguiente:

El Congreso Panamericano aprueba la idea de la uniformación de la fecha de los censos de población y encarga al Instituto de la Unión Panamericana presentar en el próximo congreso un proyecto completo sobre la materia.

CONCLUSIONES.

En vista de lo expuesto en los capítulos respectivos, el Segundo Congreso Científico Panamericano, aprueba las siguientes conclusiones:

1°. Las estadísticas demográficas panamericanas comprenderán únicamente los datos que se refieren a los matrimonios, nacimientos, nacidos—muertos y defunciones. (Antecedentes Parte IV del texto.)

2°. Se adopta la siguiente definicion panamericana de la demografía. "Entiéndese por demografía la ciencia que trata de la descripción de los pueblos según sus principales acontecimientos naturales y legales, y en cuanto estos últimos a la nupcialidad se refieren." (Antecedentes Parte V del texto.)

3°. Los países panamericanos formarán su estadística demográfica en la forma e idioma que lo estimen conveniente; pero tendrán la obligación de hacer figurar en un capítulo o folleto especial las informaciones demográficas en la forma e idioma acordados por el Congreso. Este capítulo se titulará "Informaciones demográficas acordadas por el Congreso panamericano. (Antecedentes Parte VI del texto.)

4°. Los datos que comprenderá el capítulo o folleto titulado informaciones demográficas acordadas por el Segundo Congreso Científico Panamericano serán las que se detallan en los formularios adjuntos. (Antecedentes Parte VII del texto.)

5°. Se aprueba la idea de la uniformación de las fecha de levantamiento de los censos de población de los países panamericanos y se comisiona al Instituto de la Unión Panamericana para presentar en el próximo Congreso un proyecto completo sobre la materia. (Antecedentes Parte VIII.)

Informaciones demográficas apropuestas al Segundo Congreso Científico Panamericano.

MATRIMONIOS.

FORMULARIO 1.

Matrimonios según el grado de parentesco.	Número de matrimonios.		
	Urbana (en las ciudades).	Rural (en los campos).	Total (reunidos).
Entre primos-hermanos			
Entre tío y sobrina			
Entre tía y sobrino			
Entre otros parientes			
Entre personas extrañas			
Total			

FORMULARIO 2.

Matrimonios según la nacionalidad.	Número de matrimonios.		
	Urbana (en las ciudades).	Rural (en los campos).	Total (reunidos).
Entre extranjeros			
Entre nacionales			
Entre esposos nacionales y esposas extranjeras			
Entre esposos extranjeros y esposas nacionales			
Total			

Edad media de los esposos y esposas: Parte urbana ..... Parte rural .....

Informaciones demográficas apropuestas al Segundo Congreso Científico Panamericano—Continúa.

NACIMIENTOS.

FORMULARIO 3.

Legitimidad.	Número de nacidos.							
	Urbana.			Rural.			Total.	
	Masculino.	Femenino.	Total.	Masculino.	Femenino.	Total.	Masculino.	Femenino.
Legítimos								
Ilegítimos								
Total								

FORMULARIO 4.

Legitimidad según la nacionalidad de los padres.	Número de nacidos.							
	Urbana.			Rural.			Total (reunidos).	
	Masculino.	Femenino.	Total.	Masculino.	Femenino.	Total.	Masculino.	Femenino.
Ambos padres nacionales:								
Legítimos								
Ilegítimos								
Total								
Ambos padres extranjeros:								
Legítimos								
Ilegítimos								
Total								
Padres extranjeros madres nacionales:								
Legítimos								
Ilegítimos								
Total								
Padres nacionales. Madres extranjeras:								
Legítimos								
Ilegítimos								
Total								
Otras:								
Legítimos								
Ilegítimos								
Total								

FORMULARIO 5.

Clase de partos.	Número de nacidos.							
	Urbana.			Rural.			Total (reunidos).	
	Masculino.	Femenino.	Total.	Masculino.	Femenino.	Total.	Masculino.	Femenino.
Simples								
Dobles								
Triples								
Cuádruples								
Total								

Informaciones demográficas apropuestas al Segundo Congreso Científico Panamericano—Continúa.

NACIDOS MUERTOS.

FORMULARIO 6.

Legitimidad.	Número de nacidos muertos.							
	Urbana.			Rural.			Total (reunidos).	
	Masculino.	Femenino.	Total.	Masculino.	Femenino.	Total.	Masculino.	Femenino.
Legítimos								
Ilegítimos								
Total								

DEFUNCIONES.

FORMULARIO 7.

[U=parte urbana. R=parte rural.]

Causas de muerte (nomenclatura internacional).		Edad y sexo.									
		Menores de un año.		De un año.		De dos años.		De tres años.		De cuatro años.	
		Masculino.	Femenino.	Masculino.	Femenino.	Masculino.	Femenino.	Masculino.	Femenino.	Masculino.	Femenino.
1. Fiebre tifoidea.	U										
	R										
2. Etc.	U										
	R										
3. Etc.	U										
	R										
4. Etc.	U										
	R										

Causas de muerte (nomenclatura internacional).		Edad y sexo.									
		De cinco años.		Igual año por año hasta 99 años.		De 100 años adelante.		No clasificados.		Total.	
		Masculino.	Femenino.	Masculino.	Femenino.	Masculino.	Femenino.	Masculino.	Femenino.	Masculino.	Femenino.
1. Fiebre tifoidea.	U										
	R										
2. Etc.	U										
	R										
3. Etc.	U										
	R										
4. Etc.	U										
	R										

Informaciones demográficas apropuestas al Segundo Congreso Científico Panamericano—Continúa.

DEFUNCIONES—Continúa.

FORMULARIO 8.

Estado civil de los fallecidos.	Urbana.			Rural.			Total.	
	Masculino.	Femenino.	Total.	Masculino.	Femenino.	Total.	Masculino.	Femenino.
Solteros								
Casados								
Viudos								
Divorciados								
Sin especificar								
Total								

MORTALIDAD DE MENORES DE UN AÑO.

FORMULARIO 9.

[U=parte urbana. R=parte rural.]

Causas de muerte (nomenclatura internacional).		Edad y sexo.									
		Menores de un mes.		De un mes.		De dos meses.		De tres meses.		De cuatro meses.	
		Masculino.	Femenino.	Masculino.	Femenino.	Masculino.	Femenino.	Masculino.	Femenino.	Masculino.	Femenino.
1. Fiebre tifoidea.	U										
	R										
2. Tifus exantemático.	U										
	R										
3. Fiebre recurrente, etc.	U										
	R										

Causas de muerte (nomenclatura internacional).		Edad y sexo.							
		De cinco meses.		Igual mes a mes hasta 12 meses menos un día.		No clasificados.		Total.	
		Masculino.	Femenino.	Masculino.	Femenino.	Masculino.	Femenino.	Masculino.	Femenino.
1. Fiebre tifoidea	U								
	R								
2. Tifus exantemático	U								
	R								
3. Fiebre recurrente, etc	U								
	R								

FORMULARIO 10.

Causas de muerte (nomenclatura internacional).	Meses.					
	Enero.	Febrero.	Marzo.	Abril.	Mayo.	Igual mes a mes hasta diciembre.

Informaciones demográficas apropuestas al Segundo Congreso Científico Panamericano—Continúa.

MORTALIDAD DE MENORES DE UN AÑO—Continúa.

FORMULARIO 11.

Edades.	Meses.					
	Enero.	Febrero.	Marzo.	Abril.	Mayo.	Igual mes a mes hasta diciembre.
Menores de un mes						
De 1 mes						
2 meses						
3 meses						
4 meses						
5 meses						
De adelante mes a mes hasta 12 meses menos un día						
Sin clasificación						
Total						

INFORME SOBRE EL DESARROLLO DE LA ESTADÍSTICA DEMOGRÁFICA EN LA REPÚBLICA DE EL SALVADOR,

Por PEDRO S. FONSECA,

Director General de Estadística de El Salvador.

ANTECEDENTES HISTÓRICOS.

Durante la dominación española, poco o ninguna atención mereció el ramo de estadística; se exceptúa el censo practicado en 1778, que dió a conocer que las Provincias de San Salvador y Sonsonate tenían 146,684 habitantes.

Después de la Independencia, hubo algunos indicios de trabajos estadísticos, como los ordenados en 1829, 1834 y 1837 sobre censo de población y riqueza pública, los que se publicaron en el periódico oficial sin orden cronológico. Antes de la fundación de un centro directivo, el trabajo más digno de consideración es el efectuado por el Dr. José C. López, en 1878, levantando un censo bastante aceptable.

En 1881 se fundó la Dirección General de Estadística,suspendida algunos años después y reconstituída formalmente en 1901.

Han sido Directores de Estadística sucesivamente, los Sres. Marcos Alfaro, Esteban Castro, Rafael Reyes, Francisco E. Galindo, Ramón Uriarte, Julián Escoto, Santiago I. Barberena y el infrascrito. Se han levantado censos en los siguientes años: 1778, 1878, 1882, 1888, 1892, 1896 y 1901. Algunos de ellos se consideraron inaceptables y no se dió a conocer su resultado. Es indispensable levantar un censo con plan científico y con recursos y tiempo suficiente para su preparación.

ESTADO ACTUAL.

Desde 1901 se ha podido llevar sin interrupción la estadística de nacimientos, matrimonios y defunciones. En 1911 se modificaron los modelos, procurando en cuanto es posible, seguir las prácticas internacionales. Para indicar las causas de defunción tropezamos con el inconveniente de que la mayoría de los que mueren es sin asistencia médica, razón por la cual los diagnósticos no deben aceptarse con rigorismo científico. En los cuadros de nacimientos se hace constar: El sexo, condición

legal, nacionalidad del padre (cuando el niño es legítimo y de la madre cuando es ilegítimo), si es parto único o nó, si nació vivo o muerto.

En las defunciones: Sexo, edad (se distribuye por períodos), estado civil, ocupación. causa de defunción (se agrupan conforme la clasificación de Bertillon), nacionalidad, si tuvo o no asistencia médica.

En los matrimonios: Edad, estado civil anterior, nacionalidad e instrucción de cada uno de los esposos.

El circuito demográfico es el Departamento; agrupados todos los de la República éstos se totalizan.

La dirección examina parcialmente cada uno de los informes de los 252 pueblos de la República, rectifica errores para formar el cuadro general del mes.

Los resultados se publican en el Anuario Estadístico.

He aquí un resumen del movimiento demográfico en El Salvador, durante el período de 1899 a 1914:

Años.	Nacimientos.			Defunciones.			Matrimonios.
	Varones.	Mujeres.	Totales.	Varones.	Mujeres.	Totales.	No. total.
1899	19,974	19,012	38,986	10,024	8,882	18,906	3,410
1900	21,612	20,340	41,952	9,229	8,235	17,464	2,822
1901	21,569	20,818	42,387	10,460	9,897	20,357	3,774
1902	20,788	20,217	41,005	11,456	10,907	22,363	3,402
1903	22,595	21,193	43,788	13,408	12,999	26,407	4,435
1904	22,973	21,581	44,554	11,624	11,061	22,685	4,483
1905	22,839	21,756	44,595	12,730	12,120	24,850	4,280
1906	21,731	21,093	42,824	12,384	11,696	24,080	3,578
1907	22,561	21,660	44,221	12,939	11,502	24,441	3,878
1908	24,396	23,255	47,651	12,544	12,147	24,691	4,137
1909	24,137	23,637	47,774	12,912	12,422	25,334	4,352
1910	23,845	23,021	46,866	13,886	13,467	27,353	4,287
1911	25,028	24,157	49,185	13,856	13,082	26,938	4,445
1912	25,498	24,501	49,999	12,788	12,137	24,925	4,481
1913	25,969	25,027	50,996	13,045	12,096	25,141	4,762
1914	26,374	25,485	51,859	13,046	12,367	25,413	4,013
	371,889	356,753	728,642	196,331	185,017	381,348	64,549
Media	23,243	22,297	45,540	12,270	11,563	23,834	4,034

Mediante el cálculo respectivo, se ha podido obtener el índice de natalidad, mortalidad y nupcialidad, de la manera siguiente: Nacimientos, por 1,000 habitantes, 41.66; defunciones, por 1,000 habitantes, 21.00; matrimonios, por 1,000 habitantes, 3.71.

El estado civil de los nacidos, por término medio es: Legítimos, 46.3 por ciento; ilegítimos, 53.7 por ciento; total, 100.

El máximum de nacimientos se verifica en enero, y el mínimum en junio. E máximum de defunciones se verifica en octubre, y el mímimum en febrero.

El Consejo Superior de Salubridad, lleva estadística detallada de las causas de defunciones, correspondientes a la Ciudad de San Salvador y a los puertos.

Adjournment.

GENERAL SESSION OF SECTION VIII.

NEW EBBITT HOTEL,
Wednesday morning, January 5, 1916.

Chairman, WILLIAM C. GORGAS.

The session was called to order at 9 o'clock by the chairman.

The CHAIRMAN. Dr. Weil, I think you are to start this program for us.

ANAPHYLAXIS.

By RICHARD WEIL,
Cornell University, Medical College, New York City.

I have been asked, in the unavoidable absence of Dr. Anderson, to speak on the development of the subject of anaphylaxis; that is, to give an historical oversight. I will attempt to summarize the history of its development in as few words as possible and to indicate as far as I can the main problems which have presented themselves to the men who were active in the study of anaphylaxis at the various stages of its development.

As you know, the entire literature of anaphylaxis does not go back more than 15 years. It started with a series of observations made in different parts of the world, which curiously enough foreshadowed the various phases of development which the history of anaphylaxis has taken since that time. In the first place, there was the observation of Rosenau and Anderson, in 1906, which was also made independently by others, that guinea pigs which had been given a preliminary dose of foreign protein responded to a subsequent dose of that foreign protein with severe and often fatal symptoms. That was the guinea pig phenomenon and represented the constitutional reaction of anaphylaxis. The first experiment of this type had been performed on dogs in 1902 by Richet.

The second observation, made by Arthus in Lausanne, in Switzerland, involves the principle of the local reaction. He found that rabbits which had been given foreign protein, such as egg albumin or horse serum, over a period of days, subsequently responded to later injections with a peculiar, characteristic reaction at the site of injection. They developed a severe local reaction, which might take the form of simple erythema, but might go on to abscess formation and necrosis.

The third observation was the observation of Von Pirquet that human beings who had been vaccinated once responded to a second vaccination in an altogether different way, and that was the beginning of the observations that led Von Pirquet to interpret the various manifestations of the infectious diseases upon the basis of what he called allergy, which is a somewhat broader thing than what we call anaphylaxis.

The very first problem which presented itself and which occupied the minds of investigators for a number of years was this: What is the character and what is the mechanism of the reaction? In specific terms is it an antibody reaction or is it not an antibody reaction? This recalls the violent polemic which occupied the earlier

years and in which Gay and Southard, on the one hand, and Rosenau and Anderson, on the other, played the prominent parts. Gay and Southard, as you remember, believed that when a foreign protein, say horse serum, was injected into a guinea pig, that a certain part of it remained in the body and rendered it hypersusceptible. They called this fraction anaphylactin. Rosenau and Anderson, on the other hand, were the first to maintain and defend successfully the theory that what we really had in anaphylaxis was nothing but an immune reaction. In other words, they showed that the injection of the foreign protein resulted in the production of antibodies in the guinea pig, and that the second injection permitted an interaction between this newly formed antibody and the reintroduced antigen in the body of the animal. I need hardly remind you that this controversy raged for two or three years. It was definitely settled not only through the work of Rosenau and Anderson, but with the help of Otto, working in Ehrlich's laboratory, and of others in favor of the theory of Rosenau and Anderson that the anaphylactic reaction is immune reaction.

The second question naturally involved the nature of this antibody. Was it an antibody sui generis, different in nature from what we had previously worked with, or was it essentially similar to the various precipitins, agglutinins, and so forth, with which men were already familiar? This is a controversy which has not yet been entirely settled. In my paper to-day I hope to make a contribution to that question. Friedberger was the first to maintain that the anaphylactic antibody, which has been called by various terms, "sensibilisin," etc., is identical with the precipitins. The chief argument which he advanced was that if one studies the sera of immunized animals, one finds that the precipitin content goes parallel with the passively sensitizing value of that serum, and this observation was confirmed by Doerr, who, as you know is one of the most active and successful workers in anaphylaxis. It was disputed by others. Kraus, who is now in Argentina, attacked the theory by showing that the blood of guinea pigs which have been sensitized contains no precipitins, so, as I have said, at this time the nature of anaphylactic antibody is still somewhat in doubt.

The third main problem which has busied the workers in anaphylaxis concerns the site of the reaction. Where does the anaphylactic reaction occur? I might explain this question more in detail as follows: If we admit, as we are all now ready to do, that anaphylaxis is the result of a reaction in the living body between antibody and antigen, where do these two substances unite in the body? Thinkers on this problem are divided into two schools: First, there is the humoral school, which holds that the reaction occurs in the blood. This theory is intimately connected with the so-called anaphylatoxin theory, because those who maintain that the reaction occurs in the blood—and I think that Friedemann was practically the first to advance this opinion, although it has been developed to its greatest extent by Friedberger—maintain at the same time that this reaction results in the production of a toxic substance, called anaphylatoxin, which, by its irritant action upon the cells of the body gives rise to the typical anaphylactic symptoms, the convulsions, etc. This, then, is the humoral theory.

The second theory of the site of the anaphylactic reaction is what might be called the cellular theory, which is opposed absolutely to the humoral theory and also excludes the intervention of anaphylatoxin. The cellular theory, historically, really goes back, I should say, to the French school, to Besredka, who maintained, however, that the reaction occurred exclusively in the brain cells, whereas those who now accept the cellular theory include the cells of many other tissues of the body. This theory is based very largely on the observed response of the muscle cells of the isolated uterus to antigen. According to this interpretation, antigen-antibody reactions occurring in the blood are entirely unproductive of symptoms, and are only effective when mediated by the cells of the body.

The cellular theory is at first sight not in itself incompatible with a belief in anaphylatoxin. It is perfectly conceivable that within the cells the reaction of antibody and antigen should give rise to a toxic substance, which we may call for convenience anaphylatoxin; but the development of the cellular theory has precluded such an interpretation. Dale has advanced the following argument on that aspect of the problem: The uterus of a normal guinea pig when suspended in a neutral solution, such as Locke's fluid or Ringer's fluid, and attached to a writing lever which runs upon a drum, describes a regular and characteristic series of rhythmical contractions. If one takes the uterus of a guinea pig which has been sensitized, say, to horse serum, suspends it in this way, allows it to write its tracing, and then adds horse serum to the bath, the uterus at once executes a violent contraction, and the curve shoots up at once. Now, there are several reasons for believing that this reaction can not be due to the production of a chemical substance. Dale himself showed that the reaction had no determinable latent period. He concluded that it is inconceivable on physiological grounds that the production of a secondary chemical substance by ferment action should take place with such rapidity. He stated also that the result produced in the living animal could not conceivably be due to a chemical substance formed from such minute amounts as one-ten thousandths of a gram of protein, which we know will produce the anaphylactic reaction.

These views of Dale have been accepted by physiologists. Bayliss, for example, in his last book, Principles of General Physiology, states that he also believes that it is inconceivable that the chemical reaction should mediate and precede the anaphylactic response. But the other argument is very much stronger. Doerr has shown, and those coming after him, of whom I am one, have emphasized the fact that you can not get the anaphylactic reaction if you introduce into the opposite jugular veins of a guinea pig antigen and antibody simultaneously. Now there you have the ideal conditions for reaction in the blood stream, antigen and antibody coming together, and yet nothing happens. On the other hand, the uterus of a guinea pig which has been washed out with a liter of solution and contains no blood reacts violently to antigen. If one accepts the cellular theory, one is practically bound thereby to reject the anaphylatoxin or chemical theory and to accept what has been called the physical theory.

And that brings me to the fourth problem, which I wish to sketch—the problem of the immune mechanism. When I speak of the immune mechanism I am not speaking of the gross physiological mechanism, whether it be spasm of the bronchial muscles or what not, but to the cellular mechanism. Are we dealing with a chemical reaction, in which the reaction of antigen and antibody results in the production of a third toxic substance, a so-called anaphylatoxin? Or are we dealing with what has been called a purely physical process—in other words, something like an electric shock, whereby the sensitized cell, simply in virtue of the presence of antigen, without any intermediate change, is at once stimulated to the discharge of its normal activities—resulting in the case of the uterus in a contraction, in the central nervous system in convulsions, such as strychnin produces, and so forth.

As I say, those two theories are incompatible, and they are each of them bound up either with the humoral theory or with the cellular theory. I do not wish to go too far into a discussion of this subject, in view of the fact that there are to be several papers which bear upon it, and also because my own views are too strong to allow me to give you a perfectly impartial historical résumé of it.

In regard to the practical application of our knowledge of anaphylaxis, I believe we are probably at the very beginning of our understanding of the relation of the phenomenon to disease. The beginnings were sketched by Pirquet and Schick, who attempted to interpret the various phenomena of the infectious diseases upon the theory of an anaphylactic reaction; the incubation stage corresponded to the

period in which the animal was developing its antibodies, just exactly as a guinea pig after receiving an injection of horse serum is apparently unaltered during an interval of 10 or more days and then makes an acute response to the reintroduced antigen. If the production of the antibodies is violent and in large amounts, we may have an initial chill; if not, a gradual onset. Pirquet and Schick also took up the question of the local diagnostic response, such as the tuberculin reaction, and attempted to explain it upon the theory of the anaphylactic phenomenon—viz, that the immune animal responded with a locally excessive response to the introduction of the antigen.

Those theories, although they have been rather generally accepted, have still met with a good deal of opposition, and require a good deal in the way of elucidation. If we come to the most prominent problem, we might say, which confronts all medical men—viz, the specific diagnostic reactions, such as the tuberculin reaction or even the secondary vaccination response—we know very little as to the mechanism. We do not know whether that response is due to the cellular reaction—whether the cells of the body are furnished with antibodies and mediate the response, or whether it is due to simply the presence of antibodies in the blood. The same holds true of the interpretation of the Arthus phenomena. Notwithstanding these difficulties, the whole fabric of the infectious diseases is by many believed to be interpretable upon an anaphylactic basis. This has gone so far that certain observers have maintained that the evolution of even the chronic infectious diseases is essentially referable to anaphylactic laws. For example, they maintain that the reason tuberculosis in infants is found at autopsy very largely to take the form of a general miliary tuberculosis, whereas in adult life it generally observes an altogether different distribution—namely that of a localized process—is simply the fact that the infant has not developed resistance through the formation of antibodies and the infection consequently spreads through the system. In the same way they point out that in the secondaries of syphilis one has generalized manifestations of disease, whereas in the late stages of the disease one has some localized lesion, and they maintain that the individual infected with lues develops the typical secondaries because he has no antibodies, but as the disease progresses (just as in the case of an adult who has gone through tuberculosis early in life and has a second infection later in life), the reaction is altogether different, owing to intervening production of antibodies. So these men maintain that in the development not only of the acute but of the chronic diseases we are dealing with conditions that have been produced through the altered reaction of the host to the infecting organism.

One might really go on, I suppose, almost indefinitely, developing the various tendencies in the interpretation of disease through anaphylaxis. Of course, you all know that certain diseases, such as the food idiosyncrasies, hay fever, etc., are now quite thoroughly explained upon the anaphylactic basis. But we have a fairly long program, and I, unfortunately, had no time to prepare this talk, being told only just before the meeting began that I should have to give it; so I think that we may now conclude this general resumé, and proceed to the special papers of the program.

Dr. Richard Weil took the chair and announced a paper on "The Argentine biological theory of immunity" by Dr. Julio Méndez. This paper, previously printed in the Revista de Filosofía, año 1, núm. v, septiembre de 1915, was submitted to the congress through the courtesy of Dr. Ricardo Sarmiento-Lespiur and read by him at this session.

TEORÍA BIOLÓGICA DE LA INMUNIDAD.

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I.

El organismo animal posee dos grandes grupos de funciones. Uno corresponde a los fenómenos de la vida de relación. El otro corresponde a los de la vida vegetativa.

Dentro de estos últimos encuadran; los actos de la nutrición, propiamente dicha, que intervienen en la asimilación o adaptación de las substancias digeridas, y que tienen por objeto la regeneración de nuestros órganos y tejidos, desgastados constantemente por el funcionamiento vital; y los actos que intervienen en los procesos patológicos, que al contrario de los anteriores tienen por objeto la alteración estructural de esos mismos órganos y tejidos, provocando la enfermedad o la muerte.

Hasta hoy no nos hemos preocupado de estudiar o comprobar el lazo de unión que existe entre ambos actos, atraídos por los nuevos fenómenos descubiertos en el ambiente patológico, que en estas dos últimas décadas ha realizado progresos incalculables.

Antes de empezar a tratar de ellos en el presente artículo, conviene saber, a manera de orientación para seguir nuestras ideas, que el sistema vegetativo del organismo y los actos que él rige, o sean las mutaciones intra-orgánicas, obedecen a un solo y único proceso, sea cual fuere la vía por la cual la substancia se introduce. Estas vías son: la enteral o gastro-intestinal y la para-enteral (circulatoria, subcutánea, nerviosa o linfática).

Que la substancia sea propiamente alimenticia, como las albúminas de la digestión de nuestros alimentos, o sea patológica, como los gérmenes de las enfermedades que nos atacan, el acto o los fenómenos a que da lugar la adaptación de ellas por el organismo (para que lleguen a formar parte del mismo o a alterarlo provocando la enfermedad) es perfectamente idéntico, diferenciándose, como es lógico, en sus efectos. Esta unidad de acción dentro del organismo animal no ha sido aún sancionada por la ciencia, siendo sin embargo una realidad demostrada en cada uno de los miles de experimentos que se realizan y que vienen a satisfacer la lógica del biólogo, descubriendo en todos esos actos fenómenos físico-químicos, sometidos, como las reacciones que provocan, a un determinismo ineludible. En efecto, no es dable suponer a quien conoce el funcionamiento del organismo animal, que la asimilación de las albúminas digeridas de carne de pescado, por ejemplo, sea distinta de la asimilación de las similares de carne de vaca. O, en otras palabras, que el mecanismo usado por el organismo se modifique de manera distinta para la adaptación de una u otra.

Aparte de la infinita variedad de modificaciones funcionales que exigiría, dada la variedad de los productos presentados, tal creencia nos llevaría al absurdo de pensar que en la escala zoológica existen más grandes diferencias en el terreno vegetativo que las que evidentemente existen en la de los órganos de la vida de relación.

Así, dentro del organismo, los actos que rigen la asimilación de las albúminas alimenticias y los que rigen la asimilación de las albúminas patógenas, son perfectamente idénticos. El organismo se desarrolla y se mantiene por el mismo procedimiento que se enferma. La nutrición y la enfermedad son procesos biológicos idénticos.

II.

Lo que acabamos de esbozar interesa sumamente al biólogo, al médico y aun a los que deseen tener una idea de esa mecánica fisiológica que significa el equilibrio vital.

Para la teoría biológica de la inmunidad, es la base que ha permitido a esta teoría adelantarse por muchos años al estado actual de los conocimientos respectivos.

Desde que el proceso de la nutrición íntima y el de la enfermedad son idénticos como actos biológicos, y habiendo la investigación penetrado o detallado más los concernientes a la enfermedad, estudiemos ésta, aunque de manera somera, para acentuar el detalle más tarde, al tratar de la inmunidad, que es una de sus consecuencias.

Cuando un individuo se enferma, de enfermedad infecciosa (o si quiere por causa venida de fuera del organismo), necesita que el agente causante o microorganismo haya penetrado en sus tejidos (contagio) por una vía cualquiera, ya enteral o ya parenteral. Este microorganismo o germen, permanece como "cuerpo extraño" dentro del organismo, hasta tanto se verifiquen en su alrededor los fenómenos que van a asimilarlo, para que el portador sufra los trastornos de su especificidad.

Al período latente en que se desarrollan esos fenómenos se llama incubación, y está constituída por lo que Metchnikoff ha sido el primero en demostrar bajo el nombre de "Fagocitosis," que consiste en el atrapamiento de los gérmenes por los leucocitos o glóbulos blancos de la sangre, atraídos al sitio por el acto reflejo que motiva la presencia del hasta ese momento "cuerpo extraño." Los leucocitos se extravasan de los vasos capilares de la región y se dirigen con más o menos atracción hacia él, enviándoles sus pseudopodios o prolongaciones protoplasmáticas, que concluyen por atraparlo e introducirlo dentro del glóbulo blanco. El fenómeno se continúa gradualmente y puede ser seguido en preparaciones microscópicas coloreadas, en todas sus fases, observándose que después de un tiempo el germen comienza a colorearse más difusamente, luego pierde su forma y por fin desaparece, confundiéndose con el protoplasma del leucocito, que soporta también cambios concomitantes que disgregan su protoplasma haciéndole menos electivo a las sustancias coloreantes, y terminan por la deformación del o de los núcleos del fagocito, que desaparece en el suero exudado al través de los capilares (fagolisis).

Otras veces la incubación está constituída por una análoga transformación de los gérmenes, sin la presencia de los leucocitos, por el suero de la sangre extravasada de los capilares. En este caso no se observa fagocitosis; hay destrucción por el líquido solamente: bacteriolysis o fenómeno de Pfeiffer.

Tanto la fagocitosis como la bacteriolysis existen en un mismo acto, predominando una u otra según la mayor o menor virulencia del microorganismo que se ha introducido; así lo hemos demostrado en un experimento fundamental, el año 1900, bajo el nombre de "Cuadros de la infección" y que ha sido el primer paso de nuestra teoría, logrando al mismo tiempo asociar las dos doctrinas de Metchnikoff y Pfeiffer, reñidas y combatientes por largo tiempo en aquella época de la bacteriología.

El resultado de esta digestión de los gérmenes, como se ha dado en llamarle, es la destrucción de unos y otros, gérmenes y fagocitos, parcial o total, de lo que resulta la producción de anticuerpos.

Hasta aquí lo clásico. Pero ¿cómo obran estos anticuerpos? ¿cómo actúan los gérmenes para producir la fiebre, el malestar orgánico, la alteración de función y de estructura de tal o cuál órgano? No se sabe.

El adelanto en esta rama se ha bifurcado en dos direcciones. La una instigada por los célebres trabajos de Ehrlich que absorbieron la atención de los observadores, y paralizaron la investigación en la otra. Estos trabajos lograron demostrar las reacciones que individualizan a los anticuerpos, llegando a determinar con hipótesis brillantes tomadas del concepto químico, la composición, o mejor dicho, la agrupación de sus componentes. Así conocemos el amboceptor, los receptores y el componente, que explican el encadenamiento de los anticuerpos con los gérmenes o substancias que le dan origen y cuyo conocimiento, juntamente con las investigaciones de la otra bifurcación, a que nos hemos referido, llegan a la individualización de los distintos anticuerpos conocidos con el nombre de aglutininas, precipitinas, opsoninas o bacteriotropinas, etc.

Estos anticuerpos existen en el suero de la sangre de aquellos animales que han pasado el contagio espontáneo o experimental de gérmenes, y por sus propiedades estrictamente específicas poseen la cualidad de que, puestos en presencia de dichos gérmenes o substancias de origen, los aglutinan, los precipitan, los atraen, etc., como se demuestra por reacciones in vitro.

El conocimiento de las propiedades antedichas, con cualidades esenciales y por consiguiente perfectamente específicas respecto del cuerpo de origen, ha desarrollado

una amplia y considerable vía dentro de la Medicina, fundando el diagnóstico biológico casi matemático, que tan inconmensurables servicios está prestando a nuestra ciencia, sacándola del estancamiento en que la había postrado el síntoma y la terapéutica sintomática.

Para ese conocimiento clásico moderno, los anticuerpos no prestan otro servicio que el de brillantes y seguros medios de diagnóstico.

Reclamamos aquí la atención del lector sobre lo que dejamos dicho, porque al desarrollar más tarde nuestra teoría tendremos que referirnos especialmente a ésto. Queda así un gran vacío entre los conocimientos clásicos actuales de los anticuerpos y la producción de las antitoxinas, cuerpos estos últimos que evidentemente existen, pero cuya formación no ha sido hasta hoy explicada.

III.

En el párrafo anterior hemos explicado lo que es la incubación; ahora veamos el comienzo de la enfermedad o lo que se denominan "pródromos." Se llama así a las primeras manifestaciones subjetivas de malestar para el enfermo, y a los síntomas que hacen ostensible para el médico el desequilibrio de la salud.

La interpretación que pasamos a exponer y los experimentos que relataremos en otro momento, nos pertenecen en absoluto.

A esos anticuerpos que provienen de los gérmenes o substancias de origen, no se les reconoce acción biológica dentro del organismo. Nadie sabe qué es lo que sucede después de la destrucción de gérmenes y leucocitos. Para Metchnikoff y Pfeiffer el rol importante del organismo es destruir el agente, y ven como terminado el proceso por su solo aniquilamiento.

Para nosotros, al contrario, ese acto es el comienzo de la infección del individuo. Los gérmenes transformados en su destrucción, por los leucocitos o por el suero, han perdido su forma, si se quiere, pero no sus cualidades. Transformándose unos y otros (gérmenes y fagocitos) en albúminas solubles, se combinan para formar los anticuerpos que nos ocupan. Ahora bien, dichos anticuerpos, como está clásicamente demostrado, y en parte confirmamos ampliamente, no son capaces de provocar ningún fenómeno patológico dentro del organismo que los contiene. Sin embargo algo aun no conocido debe haber que sea causa de la enfermedad o muerte del sujeto. Este algo más es lo que nosotros hemos descubierto, denominándolas "Lysinas" o anticuerpos terciarios, para diferenciarlos de los anteriores, que llamamos secundarios, habiendo tomado estas últimas denominaciones de Ehrlich, sin que se equivalgan absolutamente con las de dicho autor. Ello se explica porque cuando estudiábamos estas cuestiones y las publicamos, en 1903, no teníamos la orientación que ahora poseemos, ni la nueva ciencia era rica en términos ad hoc.

Las lysinas, lo mismo que los anticuerpos secundarios o haptinas, constituídas por la destrucción del gérmen y del leucocito—pero de partes esencialmente distintas que las que sirven para constituir los secundarios, como lo conoceremos luego—son las que circulando en el organismo a medida de su producción, se adaptan a las células de los tejidos cuya estructura alteran y provocan los fenómenos funcionales que exteriorizan para nosotros los síntomas de la enfermedad.

IV.

Durante la enfermedad, los tejidos u órganos que por su afinidad han adaptado las lysinas, experimentan en períodos variables, transformaciones histológicas conocidas desde mucho tiempo. Las células, elementos de esos tejidos, se presentan a la observación microscópica en diversos estados de alteración, que se denominan: tumefacción turbia, infiltración grasosa, degeneración grasa, etc., y que desde Virchow han sido descritos como alteraciones del protoplasma celular que manifiestan el padecimiento, y respectivamente la muerte de la célula.

Paralelamente a estas alteraciones estructurales van produciéndose las funcionales, desde que el órgano celular pierde proporcionalmente las propiedades de su parénquima normal, fuente de la función que le está encomendada.

La fiebre, el dolor, la dispnea, la albuminuria, la hipotensión arterial, etc., son las consecuencias de este ataque de las lysinas a los elementos celulares de nuestros órganos.

La enfermedad constituída evoluciona de diversa manera según sea la calidad y cantidad de la lysina, según sea la categoría y funcionamiento de las células atacadas.

Aquí se vuelve a observar un fenómeno análogo al de la fagocitosis, es decir, el complejo que se constituye entre la célula y la lysina es el mismo que el del germen y el fagocito en aquélla. Pero lo que en este caso es fácil de demostrar por la morfología de los cuerpos que intervienen (gérmenes y leucocitos), en las lysinas no se puede demostrar gráficamente, porque circulan en el plasma como substancias disueltas. Y es por esto que no son conocidas por los observadores y que nosotros, habiéndolas concebido en 1903 con la claridad con que las expondremos más tarde, hemos pasado nueve años sin poder llegar a demostrarlas.

Estas lysinas y las células de tejido constituyen así nuevos cuerpos que provocan la alteración o la muerte de esas células, o bien la formación de otro nuevo anticuerpo con cualidades específicas del género de la lysina que le ha dado origen: o sea la antitoxina.

La curación o sanación se electúa por la regeneración de la célula que ha sufrido la acción de la lysina, o indirectamente por la excreción de la antitoxina.

Por la evolución de este proceso, el enfermo sanado, presenta un estado biológico refractario que constituye la inmunidad.

V.

La inmunidad es un estado orgánico que confiere al organismo animal la resistencia para soportar una infección dada, sin que ella le provoque alteración en su salud.

La inmunidad se adquiere casi sin excepción por el paso de una enfermedad. Puede ser temporaria como en la influenza, la neumonía, etc., o persistente por toda la vida como en la tifoidea, la viruela, etc. En esos casos se llama adquirida natural.

La adquirida artificial es la que logramos provocar por la introducción de gérmenes a voluntad para producir el mismo estado que en la natural, y que como ella representa un proceso de infección en que el organismo (medio) contribuye como parte principal para constituirlo.

Es necesario, antes de pasar adelante, conocer bien lo que entendemos por infección. Para nosotros, es el primer acto del fenómeno patológico que, según se desarrolle, puede llegar a provocar la inmunidad o la muerte. En los dos casos la infección se verifica efectuando reacciones idénticas que sólo varían en graduación y que demuestran, una vez más, cómo los actos biológicos del organismo obedecen a una sola y única ley.

Según nuestro modo de ver, la infección representa actos semejantes, sea que el agente infeccioso esté constituído por microrganismos o por toxinas. Esto echa por tierra el modo de ver clásico que mantenía la diferencia entre enfermedades por septicemia (ejemplo: carbunclo) y enfermedades por toxemia (ejemplo: difteria). En el primer caso el agente (microrganismo) produciría la enfermedad por la multiplicación de sus gérmenes dentro del organismo. En el segundo, la toxina o veneno soluble produciría la enfermedad por intoxicación.

Estas ideas pueden ser fácilmante combatidas, demostrando, como lo hemos hecho en los "Cuadros de la infección," que toda substancia orgánica, morfológica o no, introducida en el organismo se comporta como materia extraña e innocua, mientras no haya sido digerida por los fagocitos o el suero y transformada en anticuerpos, que son los únicos elementos que por sus cualidades biológicas excitan los intercambios orgánicos.

El hecho mecánico de la fagocitosis es fácil de comprobar al microscopio para los elementos morfológicos que la constituyen; no así el de las toxinas, líquidos informes. Pero la simple observación de la irritación local que provoca la inyección de microrganismo o toxinas bajo la piel de un animal, enseña a ver aún a los menos avezados lo que pasa después de algunas horas: un edema inflamatorio doloroso y turgente que microscópicamente se presenta en ambos casos constituído por un exudado más o menos rico en leucocitos, ofreciendo en uno el cuadro de la fagocitosis de los gérmenes aun reconocibles, y en el otro sólo los fagocitos sin forma reconocible en su interior. Besredka ha demostrado que soluciones tóxicas de arsénico inyectadas al animal, se las encuentra en mayor cantidad en el exudado rico en leucocitos que en el suero, lo que se comprueba por reacciones químicas y confirma en consecuencia que los leucocitos se apoderan de los líquidos de igual manera que de los gérmenes.

Los autores han pasado por alto esa identidad de acción de microrganismos y toxinas por no haberles concedido la atención que se merece y que hemos sido los primeros en señalar hace 15 años.

VI.

Ahora que conocemos en sus líneas generales lo que pasa dentro del organismo, cuando los agentes patógenos lo contagian, estudiemos con detalle las substancias que toman origen por este contagio y los efectos que producen.

Los anticuerpos constituídos por la fagocitosis o la bacteriolysis son de dos especies: anticuerpos secundarios o haptinas y anticuerpos terciarios o lysinas.

Según la deducción analítica a que nos han llevado estos estudios desde sus comienzos, guiados como hemos estado siempre por la observación del hombre enfermo o del animal de experiencia; en la composición de todo microrganismo o substancia orgánica amorfa (coloide) existen dos cualidades: una, que representa las particularidades de su estroma o estructura, y que sería como la perteneciente a su membrana de envoltura o a su esqueleto de sostén, si pudiera expresarse así (ectoplasma); y la segunda a las particularidades debidas a la estructura y funcionamiento de su protoplasma (endoplasma).

Estas dos cualidades, difíciles de evidenciar por los medios físicos o químicos, se hacen ostensibles por sus propiedades biológicas; y su existencia, demostrable por la experimentación, es el hecho más fundamental de nuestra teoría.

A esos dos componentes biológicos del germen o toxina, a esas albúminas extrañas al organismo—que se denominan con el nombre genérico de "Antígeno"—se debe la formación de las dos clases de cuerpos que nos ocupan.

Para los haptinas, el ectoplasma o estroma; para las lysinas el endoplasma o substancia protoplasmática del antígeno. Ambas, en razón de su origen, tienen cualidades distintas que vamos a estudiar, y ambas llenan un rol diverso en el proceso de la inmunidad y de la enfermedad.

Hemos visto que las haptinas, después de constituídas y circulando en la sangre, gozan de propiedades específicas, caracterizadas por la atracción hacia al antígeno de origen. Es en virtud de estas propiedades que vuelven de nuevo a transformar el antígeno reintroducido al organismo en haptinas idénticas, las que siguen regenerándose durante un tiempo variable, hasta que desaparecen por diversas causas, y entre ellas por la falta de nuevo antígeno reintroducido.

La cualidad de destruir el antígeno da a estos cuerpos doble rol: 1°, aniquilar el antígeno, y por consiguiente evitar su multiplicación; 2°, coadyuvar, por el hecho de favorecer ese aniquilamiento, a la limitación en la producción de las lysinas que, constituídas, tienden fatalmente a producir la enfermedad.

La transformación que este aniquilamiento produce es el fenómeno biológico indispensable que sirve para hacer adaptar al organismo el cuerpo extraño que representa el antígeno, y que hemos denominado "animalización," a falta de una terminología más adecuada para estos actos íntimos del organismo.

De todo esto se deduce que son factores primordiales en el proceso de la inmunización como en el de la enfermedad. Sin ellos el antígeno dejaría de ser el excitante venido de fuera, y el ciclo mórbido no podría desarrollarse.

Pero donde más salta a vista este rol primordial de las haptinas, es en el ciclo de la nutrición de nuestro organismo. ¿Cómo podrían sernos útiles las albuminas de los alimentos después de la digestión química que sufren en el tubo gastro intestinal, cuando absorbidas por la sangre y por el quimo, no fueran animalizadas por las haptinas? Vendrían a ser lo que el antígeno no transformado en el ambiente patológico: "cuerpos extraños," incapaces de desarrollar el ciclo evolutivo de la nutrición.

La concepción de las haptinas en esta forma, ensancha su rol en el organismo, y vienen a ser así los factores fisiológicos de la nutrición para la vida del indivíduo, como vienen a ser los factores fisiopatológicos para la enfermedad o para la inmunización del sujeto.

Su ciclo de evolución dentro del organismo, se reduce al leucocito como centro, y son sus extremos, el antígeno que le da origen y el antígeno que de nuevo lo atrae. Ninguna célula de tejido, ningún parénquima, en una palabra, ningún órgano de la vida de relación es atacado por las haptinas.

Este rol importantísimo que les atribuímos, y sobre el que se basa casi exclusivamente el acto inmunizatorio, es negado sin reticencia por todos los autores, que sólo han profundizado el estudio de su rol de reactivos específicos, evidenciados por fenómenos in vitro. El estudio de estas reacciones iniciado por Bordet y Ehrlich, continuado por todos investigadores hasta hoy, ha despistado la atención del punto culminante que acabamos de establecer, ocultando así su alto rol biológico de agentes fisiopatológicos del organismo.

VII.

Como ya lo hemos dicho anteriormente, hemos dado el nombre de "lysinas" a los anticuerpos terciarios que se constituyen al par de las haptinas durante la fagocitosis o la bacteriolysis del endoplasma del antígeno introducido al organismo.

Hay que tener bien presente que la palabra lysina, no es nueva y que en ciencia se usa frecuentemente como sinónima de destrucción.

Así Pfeiffer fué el primero que, en estos estudios, significó la disolución o destrucción de los bacilos con el nombre de bacteriolysis. A la destrucción de los glóbulos rojos, se llama hemolysis; a la de las células, cirolysis, etc.

Nuestras lisynas, que hemos introducido por primera vez en la patología biológica, tienen cualidades propias que las caracterizan y las distinguen fundamentalmente de todos los otros cuerpos biológicos.

Formadas como las haptinas, por un fenómeno análogo, se diferencian desde ese momento mismo porque los antígenos capaces de darlas son mucho más virulentos que los necesarios para dar haptinas. También porque su formación es precedida siempre por una etapa de formación de haptinas puras, necesarias para excitar la fagocitosis de aquellas, al comienzo del acto fagocitario; gracias a esa preparación para la transformación de las lysinas podemos explicar el fenómeno de la anafilaxia, como veremos luego.

Su ciclo de acción es completamente distinto del pequeño ciclo en que se forman y actúan las haptinas. Empieza en el fagocito como aquéllas; se difunde inmediatamente de constituídas en la sangre y son atrapadas por las células de nuestros órganos con avidez sorprendente, como sucede con los venenos o ponzoñas que inmediatamente de inoculadas por la picadura de las serpientes o arañas, enferman o matan, a causa de esa difusibilidad y de la atracción de las células por ellas.

La acción de las lysinas, como nosotros las concebimos, se limita a las células de tejido, alterando su estructura y por consiguiente su funcionamiento (como lo hemos dicho al hablar de la enfermedad), y dan un producto, en los casos de regeneración total de la célula, o sea en los casos de sanación que es lo que conocemos, desde Behring, por antitoxina.

De modo que la lysina, nacida en la fagocitosis o bacteriolysis del antígeno, tiene por centro la célula de tejido y se termina por la formación de antitoxina. No es como la haptina que termina donde empieza y presenta por consiguiente las cualidades reversibles de los fermentos. La lysina, una vez formada, se encadena totalmente a la célula y no encuentra, durante su existencia como tal, ningún cuerpo con propiedades de neutralizarla.

Este es un hecho importantísimo para nuestros conocimientos de la enfermedad y de la sanación, y permite explicar el rol secundario de la antitoxina en la curación de la enfermedad, que hasta hoy no había sido detallado en todas sus fases.

Hemos repetido varias veces que la lysina es el factor de la enfermedad propiamente dicha, explicándonos su acción, en la primera época de nuestros trabajos, por simples deducciones de observación clínica y bacteriológica.

Pensábamos entonces que la enfermedad sólo la produce el antígeno virulento, es decir, según lo que hemos explicado, el antígeno que ofrezca más substancia protoplasmática; y como ésta es la que contribuye a la formación de la lysina, a mayor virulencia corresponde más cantidad y eficacia de la producción de lysina.

Pero esta hipótesis, para ser aceptada, necesitaba ser demostrada por hechos experimentales, a los que no pudimos llegar durante largo tiempo, atribuyendo la dificultad del problema a la difusibilidad y a la falta de atracción de las lysinas hacia un cuerpo que pudiera servirnos para su demostración in vitro, al igual de las reacciones descubiertas por Ehrlich para las haptinas.

Es seguramente por esta falta de atracción a todo lo que no es célula parenquimatosa, que las lysinas han pasado inadvertidas hasta nosotros.

El estudio del fenómeno de la anafilaxia nos ha permitido encontrar las reacciones demostrativas de la existencia de estos cuerpos, que pasamos a relatar sumariamente, extractando de nuestros trabajos publicados sobre la materia.

VIII.

Richet ha denominado anafilaxia al fenómeno que se observa cuando un animal inyectado con un cierto antígeno es reinyectado después de algún tiempo con el mismo antígeno; inmediatamente de la reinyección, el animal presenta un cuadro de síntomas graves, bien caracterizados, que pueden terminar por la muerte.

La anafilaxia se provoca de varias maneras.

Cuando se inyecta a un animal una dosis de antígeno mucho menor que la necesaria para producir la muerte, de modo que no altere su salud, y se inyecta de nuevo cantidades aun menores del mismo antígeno algún tiempo más tarde, se observa que inmediatamente después de la segunda inyección el animal sufre un "choc" que produce la muerte casi instantánea. Esto es lo que se llama anafilaxia activa.

Se puede producir el mismo fenómeno inyectando a un animal el suero de la sangre de otro que ha sido inoculado previamente con dosis mínima del antígeno. El animal así preparado o en estado pre-anafiláctico, al ser inyectado días después con el antígeno, sufre el "choc" idéntico al del ejemplo anterior. Se tiene entonces la anafilaxia pasiva.

Estudiando estas cuestiones, en 1910, tratamos de explicar el fenómeno de la anafilaxia al través de nuestra teoría, y para hacer más apreciable la idea, imaginamos la siguiente fórmula:

FÓRMULA DE LA ANAFILAXIA.

Primera inyección, primera faz..{Anticuerpos secundarios+(haptinas).
Anticuerpos terciarios 0 (lysinas).

Segunda inyección, segunda faz.{Anticuerpos secundarios+++(haptinas).
Anticuerpos terciarios+++(lysinas).

Interpretando, tenemos: que la primera inyección dota al organismo, después de un cierto tiempo, de abundante producción de haptinas y de muy pocas o ninguna lysina.

La segunda inyección, en virtud del estado anterior, es transformada rápidamente en ambos anticuerpos; y como de éstos las lysinas son los únicos patógenos, a ellas se debe el fenómeno.

De modo que para nosotros el "choc" anafiláctico se debe únicamente a la producción de las lysinas constituídas instantáneamente por las haptinas preformadas de la primera inyección.

Para demostrar experimentalmente esta afirmación teníamos que buscar otros ejemplos que los de la anafilaxia activa o pasiva, con objeto de penetrar al fondo del fenómeno.

Así tentamos experimentos nuevos, a fin de poder eliminar para el 'choc" anafiláctico la intervención directa del antígeno y aun del período pre-anafiláctico, es decir, prescindir de la anafilaxia activa y de la pasiva, por ser por sí mismas insuficientes.

Y es lo que hemos conseguido y demostrado en nuestro trabajo con Ceballos.

Consiste en tomar una gota de sangre o del suero de un animal, puesto en "choc" de anafilaxia activa, e inyectar esa sangre o suero en el corazón, a otro animal de la misma especie. Este último entra inmediatamente en "choc" con un cuadro de síntomas idénticos al animal proveedor. El fenómeno se obtiene evidente, ya sea con sangre pura, con suero activo o con suero inactivo.

Por esta experiencia queda suprimido el antígeno en el animal receptor, y, simplificando el problema, demuestra que por el hecho de la segunda inyección se han formado cuerpos deletéreos en el animal de origen, que circulando en la sangre pueden ser transmitidos con ella a otro animal no preparado. También se nota que este nuevo modo de anafilaxia transmitida suprime el período pre-anafiláctico.

Pero aun no es bastante para aislar las lysinas de otros cuerpos nuevos, que según Richet y otros autores se forman especialmente por la re-inyección. Estos cuerpos sui generis, imaginados ad hoc para el fenómeno anafiláctico, no existen, o por lo menos nadie los ha descrito en el proceso espontáneo de la enfermedad o en el artificial creado por la inmunización conferida. Son puramente hipotéticos, y a nuestro modo de ver ilógicos en el encadenamiento de los actos fisiopatológicos del organismo, que, como lo hemos dicho más de una vez, obedecen y se desarrollan dentro de una ley única e inmutable.

Para eliminar del todo la técnica de los autores, a la que parece atribuírsele la formación de esos nuevos cuerpos especiales, hemos verificado experimentos publicados bajo el nombre de "Experiencias de las lysinas," que consisten en inocular de una sola vez a un animal una dosis del antígeno suficiente para producir la muerte, como sucede en la infección natural. Extrayendo una pequeña cantidad de sangre, de ese animal, durante el período agónico, e inyectándola inmediatamente dentro del corazón de otro animal normal de la misma especie, provoca en éste, inmediatemente, los diversos síntomas del "choc" anafiláctico.

¿A qué se debe el "choc" en este animal receptor?

No es a la anafilaxia clásica, que exige la re-inyección del antígeno. No es tampoco a la transmitida, de Méndez y Ceballos, que aun pudiera interpretarse como el transporte de los cuerpos sui generis elaborados por el animal proveedor.

Aquí no se trata de una combinación del antígeno para producir esos cuerpos distintos del proceso inmunizante común, sino simplemente de la demostración evidente de la existencia, en la sangre del animal agónico, de una substancia constituída durante la infección de un antígeno patógeno. Y esa substancia, que conocemos en su manera de formarse, en su manera de actuar y aun en el cuerpo que constituye durante el proceso fisiopatológico de la enfermedad, es la lysina.

Si aun se duda de que el anticuerpo constituído en la enfermedad sea el mismo que el constituído en el "choc" anafiláctico, porque sus efectos parezcan distintos, en la rapidez de acción, será fácil convencerse de que no es así si tenemos presente la fórmula de la anafilaxia indicada anteriormente.

En la enfermedad, natural o provocada, la formación de lysinas se realiza gradualmente, y las células que la encadenan van recibiéndola poco a poco y produciendo con su regeneración concomitante la antitoxina; de modo que si el arribo de lysinas sobrepasa la actividad regeneradora de la célula, ésta sufre gradualmente en su estructura, como lo hemos ya explicado, y caduca al fin en el período agónico.

En la anafilaxia, la célula de tejido, virgen de todo contacto anterior con las lysinas, sufre sin preparación previa el arribo de ésta, y caduca inmediatamente por falta de actividad regeneradora.

La rapidez de los síntomas que ha sorprendido a los observadores, haciéndoles creer en fenómenos extraordinarios del organismo, entra tan exactamente en nuestra teoría que viene a ser la reacción buscada para demostrar la existencia de las lysinas (Méndez) en el organismo.

Dado que la lysina existe, y que la antitoxina (su producto de excreción) es también conocida, estudiemos someramente el rol de esta última en la curación de las enfermedades, asunto que interesa sobremanera a médicos y pacientes.

IX.

La antitoxina, descubierta por Behring para la difteria, fué en la época de su descubrimiento un gran paso que deslumbró a los estudiosos. Faltos de conocimientos suficientes entonces, atribuíasela a un simple intercambio del organismo, que transformaba la toxina inoculada en antitoxina excretada; y contribuyó aún más a esta creencia el hecho de que ambos compuestos, mezclados en proporciones adecuadas en un tubo de ensayo e inyectados conjuntamente al animal, no le provocaban malestar alguno. Luego, se dedujo que la antitoxina era el remedio específico de la enfermedad respectiva.

Efectivamente, el hecho ostensible es ese; pero, después de lo que llevamos dicho, sabemos que entre la toxina inyectada y la antitoxina elaborada, hay en el organismo un engranaje, complejo y sencillo a la vez, que permite ampliar el conocimiento de ese resultado.

En efecto, si, a manera de resumen, establecemos un cuadro en que se inscriban los nombres de todos los cuerpos que forman y constituyen el proceso patológico, relacionándolos en su evolución y afinidades, tendremos:

1. *Proceso completo.*

Primera faz; segunda faz.

Antígeno.	Fagocitosis o bacteriolysis.	Haptinas.	Haptinas y y lysinas.	Tejidos (órganos).	Enfermedad.	Curación y antitoxina.

2. *Proceso inmunizante (ciclo haptinas).*

Primera faz; segunda faz.

Antígeno.	Fagocitosis o bacteriolysis.	Haptinas.	No existe.	Antígeno.		

3. *Enfermedad (ciclo lysinas).*

Primero faz; segunda faz.

			Haptinas y lysinas	Tejidos (órganos).	Enfermedad.	Curación y antitoxina.

4. (*Ciclo antitoxinas.*)

						Antitoxina.	Antígeno.

5. *Anafilaxia.*

Antígeno.	Fagocitosis o bacteriolysis.	Primera faz, haptinas.	Segunda fas.	Tejidos (órganos).	Choc.
Reinyección.	Fagocitosis o bacteriolysis.		Haptinas y lysinas.		

El primer cuadro es resumen de lo tratado en este trabajo. El segundo indica el ciclo de las haptinas que empieza por el antígeno y concluye de nuevo en él. El tercero demuestra que la lysina constituída hace su ciclo medio hasta la antitoxina. El cuarto confirma lo clásico: la atracción de la antitoxina por la toxina.

Este último cuadro exige una explicación. En el acto patológico los fenómenos que hemos descrito se producen concomitantes los unos con los otros, o bien los unos después de los otros; por eso, en un momento dado, puede encontrarse dentro del organismo parte del antígeno aun en natura, parte transformado ya en anticuerpos. Estos pueden estar predominando en su primera faz o en su segunda. Las lysinas: en parte atrapadas por las células, en parte aun libres en la sangre. La antitoxina, formándose y excretada por las células, circulando en la sangre, en presencia de haptinas o de lysinas, con las cuales no tiene ningún rol, y siendo atraída únicamente por el antígeno al que neutraliza en el sitio de su producción.

Tomamos, por ejemplo, un enfermo de angina diftérica. En el sitío del contagio (garganta) comienza la multiplicación de bacilos que al mismo tiempo secretan la toxina respectiva. Esta es fagocitada o bacteriolizada para constituir los anticuerpos, etc. La antitoxina al fin formada, es atraída por los bacilos y por la toxina naciente que se desarrolla en la pseudo membrana, y allí la neutraliza. No hay más producció de toxina dentro del organismo y por consiguiente el contagio queda terminado. El enfermo puede quedar sano, si mientras tanto las lysinas circulantes no son activas o si las células se regeneran activamente a su excitación. En caso contrario el individuo muere a pesar de su antitoxina.

Este fenómeno explica lo que la práctica confirma día a día cuando se aplica el suero antidiftérico en los enfermos días después de comenzada la enfermedad. Cuanto más tarde es menos eficaz, porque las lysinas encadenadas por los tejidos han destruído gran parte de las células y la regeneración no es ya posible, aunque haya la cantidad máxima de antitoxina introducida circulando en la sangre. Por la misma razón es criticable la práctica en boga de inyectar dosis máximas de suero antidiftérico, creyendo que a mayor cantidad corresponde mayor efecto, cuando una dosis media es más que suficiente para neutralizar la toxina naciente en el organismo y obtener la curación si las lysinas no han alterado el protoplasma o las células de tejido.

Seguramente esta teoría no merecería ser expuesta, si no fuera más que una construcción imaginativa. Pero ella, además de ser el resultado de la observación y de la experimentación, implica una serie de consecuencias prácticas: una vez confirmada y aplicada abrirá nuevas vías a la curación de las enfermedades, constituyendo lo que hemos llamado la "Terapéutica esencial." De ella ya poseemos algunos jalones, como son: la vacuna carbuncloса argentina, el haptinógeno gono, el haptinógeno neumo, el haptinógeno tífico y otras más; hijas de las ideas vertidas en estas páginas, ejercen su acción curativa evidente de acuerdo con las consecuencias de la teoría.

Después de leída la comunicación sobre la teoría biológica argentina de la inmunidad el Dr. Sarmiento Laspiur hizo una síntesis en francés de dicho trabajo y explicó con claridad la producción del chock anafiláctico. Al terminar su disertación hizo constar que había escuchado con detención los trabajos presentados sobre anafilaxia por los delegados americanos y manifestó que ellos no eran otra cosa que

la repetición de experimentos y la descripción de los síntomas de anafilaxia, pero que en ninguno había escuchado una explicación original del fenómeno, mientras que la teoría biológica argentina daba una satisfactoria explicación del mecanismo de producción del "chock" anafiláctico absolutamente personal del Dr. Méndez.

The CHAIRMAN. The paper which has just been read is an individual way of approaching the general problem of anaphylaxis. It is difficult to discuss it owing to the terminology, which though in accord with terminology generally used differs somewhat in the interpretation of the words. As far as I can make out, the haptins and lysins are considered to be products of the antigen. The thing that specially interested me was the statement that if a drop of blood or serum is taken from an animal in shock due to active anaphylaxis and this is reinjected into the circulation of another animal of the same species, the latter animal immediately goes into shock with symptoms identical to the first animal.

I am not familiar with the original experiments of Dr. Mendez which led him to that conclusion. Similar experiments were reported a few years ago by Thiele and Embleton, of London. Now, that observation, if correct and if confirmed, is of fundamental importance in anaphylaxis and also in immunity, because if it is correct it means that substances of the type of anaphylatoxins are actually formed in anaphylactic shock and circulate in the blood as such, and you will see at once that that commits us to the acceptance of the humoral theory and to the acceptance of anaphylatoxin. It is really the one fundamental experiment to demonstrate that anaphylatoxins are formed in shock and that they are really effective.

Now, the question is whether the experiments were well made and whether the observation is acceptable. You will see that the statement made by Dr. Mendez is that a single drop of blood is taken. In the experiments of Thiele and Embleton they practically exsanguinated animals in shock. These statements as made here are not explained in detail; we do not know whether the serum was used or whether the blood was defibrinated, or whether the blood was taken into citrate. We do know that Thiele and Embleton took it into citrate and injected it very shortly afterward. Doerr has analyzed this work recently and declined to accept it, and I think for very good reasons. In the first place, he states a fact, which is really fairly well known, that blood taken from an animal in the agonal stages, in convulsions, or blood taken from any animal if fairly fresh, is highly toxic to others of the species. Why that is we do not know, but if one has had a good deal of experience in transfusing animals one comes to find that the blood of animals of the same species may be highly toxic. It is not necessary to take an animal in shock or convulsions. Now Thiele and Embleton made no controls to deter-

mine whether the blood they got from their anaphylactic animals was more highly toxic; in fact, their experiments were seriously lacking in control experiments. So, as Doerr says, we can not accept their conclusions.

Now, the statement is made here that a drop of blood produces the result. That is something entirely new, and in my experience of anaphylaxis is not confirmable, for I have more than once injected considerably more than a single drop and have never obtained the result. So there must be other factors in the experiment which I should like to hear. It seems to me this is an important point to analyze correctly, because, as I said, it plays an essential part in the question.

Dr. CLOWES. In regard to what Dr. Weil has just said, in the first place, relative to the experiments of Thiele and Embleton, citrated blood is toxic at sufficient concentration of citrate. I do not know how long ago it was originally demonstrated, but three years ago we demonstrated that .1cc m sodium citrate would kill a mouse weighing 25 grams with all the symptoms of anaphylactic shock on intravenous injection. In the second place I should like to point out that proof of the existence of anaphylatoxins is absolutely no proof that anaphylaxis is due to these substances. Anaphylaxis may well be due to a sudden and immediate disturbance of colloidal equilibrium, and I hope to demonstrate that point in the course of my work. This would correspond with the views of Dr. Weil. The subsequent production of disintegration products which in themselves appear toxic does not prove at all that the original cause of the anaphylaxis is these disintegration products.

The CHAIRMAN.—If there is no further discussion I will call on Dr. Bronfenbrenner.

SPECIFIC PARENTERAL DIGESTION AND ITS RELATION TO THE PHENOMENA OF IMMUNITY AND ANAPHYLAXIS.

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While it is generally observed that repeated injections of toxins or toxic bacterial proteins render the organism resistant against even a multiple lethal dose of said toxic substances, certain experiments have shown that under certain conditions the reinjection of even absolutely inoffensive substances may produce very severe phenomena of intoxication and even death of experimental animals. It is this exaggeration of toxicity which is the most striking phenomenon in anaphylaxis.

"Anaphylaxis is a reverse of vaccination; anaphylactic animals react to the second injection much more strongly than to the first, which is the more surprising because, in the majority of cases, the substances used are not toxic, even in very large doses,"

wrote Besredka in 1908. Where does this increased toxicity come from? Since the substances injected may by themselves be inoffensive to normal animals, even in very large doses, it is evident that conditions in the body of anaphylactic animals must be responsible for the change in tolerance to protein.

Why is it, then, that in certain cases the preliminary injection of protein raises the resistance of the animal to the subsequent introduction of the same protein, whereas in other cases it destroys even the natural tolerance of the animal, making it incomparably more vulnerable than before?

It was this loss by the animal of its normal degree of immunity or resistance to the parenteral introduction of foreign proteins which suggested to Richet the name of "Anaphylactic" for this state of hypersensitiveness of the experimental animal, following a preliminary inoculation with the foreign substance. The very name given to this phenomenon by Richet, who was one of the first investigators in this field, shows that the nature of the anaphylactic state was assumed to be quite the opposite of that of immunity or heightened resistance, in spite of the fact that both conditions seem to be brought about in the experimental animal by a very similar procedure.

It is because the parenteral introduction of foreign protein may lead in one case to immunity, and in the other to hypersensitiveness, that some authors suggested, as a working hypothesis, that the introduction of foreign protein (antigen) may lead to the formation of two independent sets of antibodies, one responsible for the heightened resistance and the other for the heightened vulnerability. These earlier theories, however, did not find confirmation in subsequent investigations.

At present the consensus of opinion among workers in this field of scientific endeavor seems to point to the assumption that, in the measure in which the development of new properties in the blood of experimental animals is responsible for the establishment of either heightened or diminished specific resistance, the same set of substances is supposed to confer these outwardly contradictory changes in tolerance of animals, to reinjection of foreign proteins.

There remains, however, an open question as to the nature of these new properties of the blood serum, as well as to the mode of their action. Still less definite is information as to the reason why these changes, brought about in experimental animals by the parenteral introduction of foreign protein, should produce a seemingly opposite effect on the natural tolerance of animals to these substances.

The changes in tolerance to a given protein, following a single or a multiple systematic introduction of the same protein into experimental animals, have been studied and variously interpreted by different investigators. But for very slight minor differences all the theories suggested can be brought back to two fundamental theoretical conceptions. One, assuming after Ehrlich, that the foreign protein, introduced parenterally into the experimental animal, is anchored by such cells of the body as happen to possess chemically active radicals (receptors), with specific chemical affinity for corresponding chemically active radicals of the protein introduced (antigen). The union of the respective radicals in virtue of their specific chemical affinity is followed by the neutralization of the chemical avidity of the cell concerned, and by the subsequent restoration and overproduction by the cell of the radicals saturated by antigen. This phenomenon (studied and described by Weigert) leads finally to the condition in which the cell finds itself overburdened with the radicals in question, and at a certain time during the process such a cell casts off into the circulation the excess of these chemically active radicals. Such substances, appearing in the circulation, as a response of the cells to the introduction of a foreign body, are known under the name of antibody. The antibodies, according to this view, retain, while free in the circulation, their power to combine with and anchor the homologous protein when such is reintroduced later. Whereas the anchoring of antigen by the specific receptors of the cell is followed by incorporation of such antigen into the body of the cell by virtue of the general digestive mechanisms of the cell, the detached receptors, circulating in the blood stream, combine with such specific antigen without digesting

it, but merely changing such antigen in a manner in which it becomes more easily attackable by leucocytes, as well as by the complement, which is supposed to be the active principle directly responsible for "cytolytic" as well as "albuminolytic" properties of the blood serum.

According to the other fundamental theory, represented best by the work of Vaughan and his collaborators, the parenteral introduction of foreign protein stimulates the production of specific ferments within the body of experimental animals. Such ferments, circulating in the blood stream, attack and digest directly the homologous protein when it is reintroduced later.

Although the above conceptions differ very substantially from each other on the question of the intimate nature of mechanisms governing the physiological processes, following the introduction of foreign protein into the animal body, both theories, in fact, indicate that such foreign protein undergoes parenteral assimilation, or digestion in the broader sense of the term, and thus eventually is eliminated from the circulation. It is this element of ridding the body of the foreign material which is responsible for the view of the whole process as a protective mechanism, especially because practically all the protein substances, when introduced parenterally, are apt to exhibit different degrees of toxicity, if the amount injected is sufficiently great.

Whichever of the two views upon the mechanisms of parenteral digestion is correct, the careful observers, beginning with Jenner in 1798 and Magendi in 1839, have noticed repeatedly that, parallel with the apparent development of specific protective mechanisms, the parenteral introduction of protein foreign to the body may give rise also to other mechanisms detrimental to the well-being of the animal.

According to the views of the school following in the footsteps of Ehrlich, the reason for such paradoxic action of parenteral introduction of protein is the fact that during the extracellular specific lysis of formed as well as unformed protein antigen in reinjected animals, this antigen is broken down through the action of complement, and the poisons preexisting in the unaltered antigen are thus liberated.

Such a view was considered especially plausible since Vaughan had shown that any protein can be broken up by chemical means, so as to yield a very powerful poison.

Friedberger, who deserves especial credit for most of the work in this direction, has shown that such poisons could be produced in the test tube by imitating the specific lysis, supposedly taking place in the body. In his earlier experiments Friedberger obtained from normal guinea-pig serum, which had been allowed to stand for some time with the washed specific precipitate (formed by rabbit serum immunized against sheep serum with the serum of the latter), very strong poisons, which killed the guinea pigs instantly with symptoms of acute shock. He named the poisonous substance anaphylatoxin, and assumed that it arose from the digestion of the specific precipitate by the ferments of normal guinea-pig serum (complement).

According to the views of Vaughan and his followers, toxic phenomena in anaphylaxia are due to the split products of direct digestion of antigen, by the specific ferments present in the blood and tissues of sensitized animals.

More recently there has appeared a great number of publications concerning the question of the mechanism of the specific parenteral digestion. Abderhalden and his collaborators who are primarily responsible for this work, have taken up the theory of specific ferments, and by using specially devised methods have seemingly demonstrated in vitro the presence of such ferments in the blood of prepared animals. These findings, if correct, seem to offer a valuable link in the chain of reasoning of the earlier supporters of the theory of specific ferments.

Approaching the question of the mechanism of anaphylaxis at this stage of its development, the investigator is confronted with a fundamental question: Assuming that the anaphylactic shock is due to the liberation of poison in the body of sensitized animals through the specific cleavage following the reinjection of antigen, what is the mechanism of this cleavage? In order to answer this question one must first determine

the nature of changes taking place in the normal physiological processes of the animal, following the first experimental parenteral introduction of the foreign protein.

On the one hand, the hypothesis of Ehrlich suggests that such parenteral introduction of foreign protein is followed by the production of specific antibodies. On the other hand, Vaughan and his followers, without definitely denying the production of antibodies, assume that parenteral introduction of foreign protein is followed by the output of specific ferments. In fact Abderhalden states definitely that the parenteral introduction of foreign protein is followed by the production of specific ferments parallel with the production of specific antibodies, but independent of the latter.

If the interpretation of the phenomena observed by Abderhalden is correct, the production of specific ferments seems to be an even more general mechanism than that of production of antibodies. For antibodies have been thus far demonstrated only, in cases of parenteral introduction of substances of animal or plant protein origin, provided that this protein is foreign to the species. Specific ferments, however, are claimed to have been demonstrated not only upon the parenteral introduction of such substances but also upon that of proteins of homologous, and even autogenous nature, provided these substances were foreign to the blood ("blutfremd"). Moreover, the parenteral introduction of substances like gelatin, pepton, cane sugar, or casein, is claimed by the Abderhalden school to produce specific ferments, capable of attacking said substances, both in vitro and in vivo. Thus the group of substances which can play the part of antigen in the production of antibody is included in that of the substances capable of causing the production of specific ferments, but is only part of it.

Such a conception of parenteral digestion, on first examination, seems very useful as a working hypothesis, for, if it is possible to prove the presence of such specific ferments, all findings from the realm of immunity can be brought into the sphere of biochemistry. The just criticism which the chemists had for a long time against the conception of immunologists who dealt with "antibodies" and "alexins"—terms which seem to name but not designate the still unknown substances—would be immediately answered.

It is thus that a number of men, familiar with phenomena of immunity, and anxious to find the general physiological principles underlying this very important mechanism, have turned their attention to the possibilities offered by the methods of investigation enunciated by Abderhalden.

In repeating the work of Abderhalden and his collaborators in this laboratory, however, we came to doubt their conclusions. Our experiments have shown that, although under certain conditions of experiment the antigen may be actually digested by the ferments of the blood of prepared animals, the ferments responsible for such digestion are not specific. In fact, as others have shown before us, the digestive ferments are present in every fresh serum, and, if set free, can digest any suitably prepared substratum in vitro without any specific predilection.

According to the findings of a number of investigators, the activity of ferments normally present in the serum is usually inhibited by a simultaneous presence of antiferments in the serum. The removal of the latter liberates the active ferments and allows digestion to take place. Indeed, Bordet, Nathan, Plaut, Flatow, and others have demonstrated quite definitely that mere mechanical adsorption by any of the substances like agar, kaolin, starch, and the like, may free serum of its antiferments and thus liberate the normal ferments.

On the other hand, as Schwartz and, more recently, Jobling and Peterson have shown, serum lipins may also inhibit the activity of normal ferments of the serum, and their removal, or, as we found it, even change in their physical state may result in activation of the normal nonspecific ferments of the serum. It is thus that a number of authors tried to explain the digestion, accredited by Abderhalden to the activity of newly produced specific ferments, by assuming that it was due to the mechanical

adsorption of antiferments by the substratum and subsequent liberation of normal nonspecific ferments. Our own experiments, however, convinced us that such is not the case. We found that although the ferments concerned in the digestion are not specific (inasmuch as they can be made to digest any substratum), the phenomenon as a whole is not devoid of a certain degree of specificity and, therefore, could not be reduced to mechanical absorption of antiferments.

Our systematic study of this question brought us to the conclusion that the element of specificity lies, not in the ferment itself, but in the mechanism of its activation; namely, we found that the apparent specificity of ferment action in vivo, assumed by Vaughan and demonstrated in vitro by the methods of Abderhalden, is due to the fact that the combination of specific serum with its corresponding antigen, in vivo as well as in vitro, is followed by a radical change in the degree of dispersion of serum colloids. This physico-chemical change in turn is followed by the activation of a normal, nonspecific ferment of the serum.

If such a conception is correct, then the phenomenon of specific parenteral digestion may be explained on a basis very similar to that offered by the chemical theory of Vaughan; but, instead of specific ferments, the digestion will be ascribed to normal nonspecific ferments, present in any fresh serum (complement) and set free by a specific mechanism of combination between the antigen and antibody (very similar to that recorded by the meiostagmin reaction of Ascoli.)

As was mentioned above, the toxic phenomena in anaphylaxis are ascribed by the chemical theory to the action of the split products of antigen, attacked by the active principle of the serum of the sensitized animal.

This hypothesis is based on observations that cleavage of the antigen in vitro by chemical means yields poisonous split products; that combination of specific serum with its corresponding antigen yields toxic substances, identical in their physiological action with those produced from the antigen chemically; and, lastly, that the actual cleavage of antigen by the ferments of specific serum can be demonstrated in vitro.

There exists, however, another view of the origin of so-called anaphylatoxin. This view represented by the work of Nolf, Doerr, Ritz and Sachs, Bordet, and others is known as "physical theory." In the main this theory suggests that the source of anaphylatoxin is not the antigen, but the protein of the serum itself.

As mentioned above, in his original experiments, Friedberger has succeeded in producing the toxic substances in vitro by a process similar to that which was supposed to be responsible for the anaphylactic shock in vivo. Namely, he allowed antigen to combine with its specific antibody and added the complement to this mixture. The poisons obtained in this manner in vitro, when injected into normal animals, were able to produce typical anaphylactic symptoms.

In his later experiments, however, Friedberger succeeded in obtaining similar poisons from bacteria and other proteins by their incubation with normal guinea-pig complement, without the concurrence of specific antibody. He still believed, however, that in these experiments also the poison was derived from the protein of the substratum. Even when Bordet, Nathan, Mutermilch, and others have been able to obtain similar poisons by the incubation of normal guinea-pig serum with agar, starch, or kaolin, and have decided, therefore, that the poison must originate from the serum, Friedberger still objected to these conclusions on the basis that these substances may contain a small amount of protein impurities, which really furnish the substratum for the formation of anaphylatoxin.

In studying this controversy one finds two really independent questions involved in it. The first question seems to be, "What are we to take to be the anaphylatoxin?" It is only after agreeing as to the exact meaning of this term that one can attack the main question, "Which is the source of poisonous substances in the anaphylatoxin formation; is it antigen or the serum?"

Originally the term anaphylatoxin was applied by Friedberger to designate the poison which was supposed to be identical with the one produced in vivo during the anaphylactic shock. This poison had two essential characteristics, making it possible to assume its identity with the substance causing anaphylaxis: First, the method of its production from combination of antigen with antibody and complement, and, second, its physiological action upon normal animals, which is identical with anaphylactic shock.

In discussing the question of the origin of anaphylatoxin different authors apparently used as criterion in their terminology only the second characteristic of the original anaphylatoxin—namely, its physiological effect upon normal animals. Thus many authors have called anaphylatoxin the chemical poisons obtained by Vaughan from bacteria. Nathan, Bordet, and Mutermilch called anaphylatoxins, substances obtained by them from the serum by adsorption with inert substances, etc. Attempts of these authors to explain the nature of anaphylatoxin seem to be generally inadequate because, even though, as my experiments have also confirmed, by digestion of serum with kaolin, for instance, one can produce from serum a substance which is similar in its physiological action, on the one hand, to the original anaphylatoxin of Friedberger, and, on the other hand, to the chemical poison of Vaughan, its identity with one or the other is not proved by this similarity alone. The identity between all these substances has to be proven before the experiments above could be taken into consideration in discussing the probable nature of anaphylatoxin.

This we attempted to do in a series of experiments in which we studied the actual mechanism of the production of poison in each instance. These experiments have shown that in the poisons arising during the incubation of the serum with kaolin or starch, as well as those arising when specific serum is digested with its antigen, the serum is the source of poisonous products. Moreover, it was found that the products of such autodigestion of serum are toxic only to homologous animals. This would indicate that during the anaphylaxis in vivo the toxic split products originate only from the digestion of serum or tissues of the animal and not from heterologous protein of the antigen (though the latter may also be attacked by the ferment at the same time).

Since it is established that in the experiments of Bordet, as well as in those of Friedberger, the formation of toxic split products is identical—namely, that it is due to the digestion by the normal serum ferments of autogenous protein—the similarity of the biologic properties of the respective end products of such digestion may speak for their identity. On the other hand, the fact that in Vaughan's experiments the poison arises from heterologous protein shows that this poison is not identical with anaphylatoxin, in spite of the similarity of its biologic action upon animals. These findings, taken in connection with the results obtained by us in the study of the mechanism of specific parenteral digestion, referred to above, suggest that the nature of anaphylatoxin is as follows: Fresh serum contains normal proteolytic ferments whose digestive action in vivo as well as in vitro is inhibited by the simultaneous presence of some antitryptic elements. This antitrypsin can be removed from the serum in vitro by two independent processes—one, nonspecific, a simple mechanical adsorption by means of excess of some organic as well as some inorganic substances; the other specific, an inactivation of the antitryptic properties of the serum, taking place as a result of the physico-chemical changes in the serum, induced by the specific interaction between the antigen and the antibody of the immune serum. The removal of the inhibiting antitryptic action of the serum by either method is followed by the restitution of the activity of the normal proteolytic enzyme, which may attack both the protein of the antigen as well as the protein of the serum itself. At a certain stage of this autodigestion the split products of the serum protein exhibit toxic properties. Biological properties of these toxic substances indicate their resemblance to the

anaphylatoxin and suggest that the anaphylatoxin of Friedberger, whether occurring in vivo or produced in vitro, is a result of the autodigestion of serum and not of the protein outside of the serum.

Our findings as cited above showed that there is no experimental evidence of the existence of specific ferments, and that the phenomena of parenteral digestion ascribed by Vaughan to the activity of specific ferments can be plausibly explained and experimentally demonstrated without assuming the existence in the body of a special specific mechanism outside of antibody formation.

Having thus answered the first question which we set out to study we will try to answer the second one—namely, that, assuming the above mechanism of parenteral digestion to be correct why, then, in some cases, the introduction of protein into normal animals results in the establishment of heightened resistance, whereas in other cases it leads to heightened vulnerability?

As we have stated above, the activation of normal ferments present in specific sera, through the changes in colloidal dispersion following the union in vivo between the antigen and antibody, may lead to digestion of antigen as well as to that of the serum itself. When the antigen mainly is digested the phenomenon is interpreted by the observer as that of protection. When the serum or other autogenous elements are digested, the split products being toxic to the animal, the intoxication occurs and the observer interprets symptoms as a sign of heightened vulnerability.

It is evident from the above that the actual mechanism of parenteral digestion in the body of the animal previously injected with the homologous protein, and thus possessing the circulating specific antibody is the same in both cases—namely, the antigen upon its reintroduction is anchored by antibody and this union leads to the liberation of normal proteolytic ferments of the serum. It is only at this point that the difference may come in, depending upon which substratum is mainly attacked by this ferment.

There must be at this point, therefore, the main problem of the situation, What determines the direction of the activity of the ferments? Is this activity selective and directed exclusively toward sensitized antigen in one case and the serum protein in the other, or is the difference in two cases only quantitative and not qualitative? Our experiments point to the second as a correct answer.

It is true some of our findings seem to show that sensitized antigen is more readily digested by the ferment in "momentu mascendi" and thus there might be a degree of selective action on the part of a ferment. But experiments in this direction are very difficult and the amount of work actually done is not yet sufficient for us to definitely claim such to be the case. On the other hand, and in the majority of experiments, there seems to be no selective action on the part of the ferment. Both the serum itself and the antigen seem to be equally subject to the attack. What, then, determines the degree of toxicity developed during this process of parenteral digestion? First of all, of course, the amount of the autogenous toxic split products liberated during digestion. And this seems to be in direct relation with the amount of antigen introduced.

It is well established experimentally that, no matter how small it may be in certain cases, the dose of antigen introduced into a sensitized animal must be sufficient to produce the anaphylactic shock. If the amount of antigen is too small the shock does not take place, although the experimental animal may show other, milder symptoms, due to partial intoxication.

It is thus evident that the amount of antigen reintroduced into a sensitized animal is a very important factor in determining the degree of intoxication.

On the other hand experiments have definitely shown that exposure of sensitized animals to cold or starvation may reduce the toxic effect of the injection of a lethal dose of antigen. These experiments suggest that not only the actual amount of antigen introduced but also the rapidity with which it unites with the antibody, may influence the rapidity of liberation of ferments and resulting intoxication. This relation may

be still better demonstrated by the known fact that if, instead of injecting at once a lethal dose of antigen into a highly sensitized animal, one would inject the same and even a larger amount very slowly, the acute anaphylactic shock might be averted. Thus the degree of toxicity developed during parenteral digestion in sensitized animals is apparently determined by the amount of digestion taking place in a unit of time, and this in turn depends on the amount of antigen injected in a unit of time.

Such a view of the phenomenon would explain, it seems, how it is that parenteral digestion, following reintroduction of antigen, may at times seemingly protect the animal, whereas at other times it injures its well-being. If the amount of antigen reintroduced into a sensitized animal is small or introduced very slowly, the amount of ferment liberated in unit of time is very slight, and the amount of autogenous split products may be so small that the animal may show no apparent symptoms of intoxication. If, however, the amount of antigen is sufficient, and if it is introduced rapidly, the rate of activation of the ferment is great and the animal succumbs of intoxication with autogenous split products.

In case of natural reinfection with pathogenic microorganisms the amount of antigen which penetrates into the body of sensitized animals is usually small enough, and even if it multiplies in the body at the beginning, the process is so slow and the extent of autodigestion in a unit of time is so slight that the reaction occurs without the visible injury to the host, and this is why the observers called the process "protective" and the animal "immune." If, however, the same animal be artificially given a large dose of the same antigen, a large amount of ferment is liberated rapidly, causing anaphylaxis, and we call the same animal "hypersensitive."

However, the amount of the antigen and the rate of its introduction into sensitized animals is apparently not the only mechanism controlling the rate of parenteral digestion as judged by the appearance of toxic split products. It is observed, for instance, that animals receiving systematic injections of toxic foreign protein at short intervals can develop their resistance to the given toxic substance to such a degree that multiple toxic dose of toxic antigen may be injected, no matter how rapidly, without producing even the slightest symptoms. It is noticed, however, that a similar animal inoculated with a similar dose of antigen, the only difference being that between the time of the last serial injection and the test injection sufficient time will elapse, will succumb with anaphylactic shock.

In both cases the amount of antigen and the rapidity of injection being the same, it is evident that the difference in time elapsed between the last serial injection and the test injection determines the difference in the effect of the respective test injections.

Just what happens in the sensitized animal during this period of time, called "incubation period," is differently explained by different authors. Our own experiments lead us to believe that the reason for the difference in the response of the sensitized animals to reinjection in the two cases cited above is as follows:

The union between the antigen and antibody, as we have suggested above, reduces the inhibiting power of the serum-antitrypsin and thus liberates its normal ferments. Such can be the case only so long as the remaining amount of antiferment is not too great to interfere with the action of the ferment as it is liberated. If the amount of antiferment is too great, it may delay or altogether prevent the digestive action of the ferments. When antigen is introduced parenterally into a normal animal once or in serial injections, such antigen is digested. It is known that the products of such digestion are strongly antitryptic. It is thus that as the digestion progresses there is going on all the time the formation of new antitryptic split products, which are eventually either assimilated by the cells in the constructive process of the body or are eliminated. Such removal of excess of antitryptic elements is, however, not rapid, and as long as the antitryptic split products of the antigen from the previous injection remain in circulation the rapid action of newly formed ferments is prevented and anaphylaxis does not occur. If, however, enough time is allowed to pass, usually about 12

to 15 days, before the test injection is given the excess of antitryptic products of previous parenteral digestion are removed and a rapid action of ferments is thus made possible. Such rapid digestion may cause the shock.

That this view is correct also follows from the analysis of the phenomenon of so-called vaccination against anaphylaxis.

It was my good fortune to study the phenomenon of anaphylaxis in Besredka's laboratory, when he found that, if the treated animal should be given a second injection of antigen before the expiration of full incubation time after the first injection, such an animal does not respond with anaphylactic shock to the test injection at the time expected (13 to 15 days after the first injection), but later. Moreover, the larger the dose of antigen injected, the longer is the state of hypersensitiveness delayed and the period of resistance prolonged. This phenomena suggested to Besredka the possibility of using it in order to avoid the undesirable reaction in anaphylactic animals. Namely, he succeeded in preventing anaphylactic shock in animals having passed the incubation period after their first or after their last serial injection by merely injecting a sublethal dose of the antigen some short time previous to the following test injection of several lethal doses of antigen. This experiment was laid in the basis of the method which is used every day now for the prevention of serum sickness in children receiving more than one injection of diphtheria antitoxin.

The mechanism of such "vaccination against anaphylaxis" was found by us to be that of retardation of ferment action by the circulating split products remaining from the digestion, following the vaccinating injection of antigen, and not to exhaustion of antibody, as assumed by others. Such a state of seeming resistance to anaphylaxis, or, as it is called, "the state of antianaphylaxis," was produced by many other procedures than vaccinating injection of antigen. Thus it was found that administration of anesthetics, sedatives, and many other toxic substances may prevent the subsequent development of anaphylaxis. The mechanism of such action of the substances just referred to was never adequately explained.

Having convinced ourselves that in the case of "vaccination" against anaphylaxis the mechanism involved was that of increase of antitrypsin, we tried to see if the same could also be true in the other cases. Actual measurements have shown this to be the case. We found that, without exception, the administration of substances known to have the effect of preventing the anaphylactic shock is followed by a more or less marked increase in antitryptic properties of the blood. Thus we suggest that administration of poisons causing destructive changes in the cells of the body, in quantities not sufficient to kill the animal outright, is followed by the death of the tissues immediately affected by the poison. With the death of tissues the intracellular ferments are set free. These ferments, possibly with the collaboration of the ferments thrown from out the surrounding fixed cells, as well as from the blood serum and leucocytes, proceed to dispose of the dead material. Some of the protein split products of such digestion, together with some of the nonprotein constituents of the destroyed cells, may exert antitryptic action. If a sensitized animal is subjected to such treatment previous to the test injection, and if such test injection is given before the antitryptic split products referred to above are eliminated, they may retard or stop the activity of proteolytic ferments liberated upon the introduction of antigen, and thus prevent the anaphylactic shock.

The view of specific parenteral digestion, as outlined in the earlier part of this paper, offers, it would seem, a plausible basis on which the various seemingly contradictory phenomena of immunity can be satisfactorily explained. Such a hypothesis suggests, first of all, that the terminology used in connection with the study of the reaction of the living organism, following its invasion by biological poisons, is not adequate.

In considering the question in the light of its historical development one is impressed by the fact that ever since the first observations on this subject the apparent increase

of tolerance to biological poisons, following their repeated introduction into experimental animals, has been accepted to be the expression of nature's protective force. This teleological conception of the reaction on the part of animal organism upon the parenteral introduction of foreign material, however, could not adequately explain all the phenomena observed. The work of Vaughn especially has suggested that in spite of the difference in the final effect the reaction of the animal body must be the same in case of heightened as well as diminished resistance to poisons. Although our experiments fully confirmed this view, the intimate mechanism of this reaction seems to us to be different from that suggested by Vaughan. There seems to be no evidence of the existence of specific ferments, and the apparent specificity of digestive processes seems to be due to the presence in sensitized animals of specific antibodies in the sense of Ehrlich.

As to the difference in final effect following the specific activation of serum ferments, it is due to the difference in rate of digestion. Thus "immunity" or "anaphylaxis" can be nothing but different forms, in which a greater and more general process of specific parenteral digestion expresses itself to the observer.

The CHAIRMAN. The next paper is by Dr. John A. Kolmer, on "The mechanism and clinical significance of anaphylactic and pseudo-anaphylactic skin reactions."

THE MECHANISM AND CLINICAL SIGNIFICANCE OF ANAPHYLACTIC AND PSEUDO-ANAPHYLACTIC SKIN REACTIONS.

By JOHN A. KOLMER,

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Among the earliest authentic records of what are now regarded as anaphylactic reactions is the description of a skin reaction by Jenner in 1798, who observed the sudden appearance of an "efflorescence of a palish red color" about the parts where variolous matter had been applied to the skin of a woman who had had cowpox 31 years before. Indeed this astute observer taught that the "disposition to sudden cuticular inflammation" following the application of smallpox or cowpox matter may be "effected by the smallpox or cowpox" and that when this sudden local reaction occurred it may be inferred that the person had had one of these diseases and was not now susceptible to either. Strangely, these observations have not attracted the attention they deserve, and even at the present day many physicians fail to recognize or consider the significance of this "immediate or immunity reaction" following cowpox vaccination among persons who are immune to cowpox and smallpox, as recently emphasized by Force.

The modern discovery of the local anaphylactic reaction is accredited to Arthus, who discovered in 1903 that the subcutaneous injection of normal serum into sensitized rabbits was followed by a local reaction at the site of injection characterized by inflammatory phenomena, of which edema was a prominent feature. At this time Arthus also showed that this local reaction was probably an expression of anaphylaxis, inasmuch as these animals would succumb with typical anaphylactic symptoms following the intravenous injection of the serum. Prior to this time Koch had observed the local reaction following the subcutaneous injection of tuberculin into tuberculous guinea pigs, but did not suspect the true nature of the phenomenon. In 1907 Von Pirquet discovered his tuberculin skin reaction and presented evidence and arguments indicating its anaphylactic nature. Since then various skin and mucous-membrane reactions have been advocated as convenient and delicate tests for the

anaphylactic state to various bacterial and other proteins, in the study of a wide group of pathological conditions.

While the earlier investigations in anaphylaxis were mostly concerned with the clinical manifestations and lesions of the condition, more recently investigators have been mainly interested in the mechanism of the phenomenon and its relation to infection and immunity. For several years my own interests in anaphylaxis have been centered upon skin reactions, and the object of this communication is to present our conceptions of the nature and mechanism of anaphylactic and other skin reactions and their clinical significance as indices of hypersusceptibility and infection and as indices of resistance to infection or reinfection.

ETIOLOGY OF SKIN REACTIONS.

Skin reactions are conducted by intradermal injection; by application to an abrasion of the skin; by rubbing into the intact skin or, as on mucous membranes, by mere contact, as instillation into the conjunctival cul-de-sac. In the first and second methods trauma due to the operation itself is a factor in the production of the resulting inflammation; likewise the intracutaneous injection of practically any protein or nonprotein substance will elicit an inflammatory reaction, providing the dose injected is large enough. The causes of various skin reactions may be summarized, therefore, somewhat as follows:

1. The true or specific anaphylactic reaction due to the interaction in the skin of specific protein antigen and specific antibody.
2. The pseudo or nonspecific protein reaction due to the interaction in the skin of general protein substances and nonspecific proteolysins.
3. The traumatic reaction consequent to the operation, or to the irritant qualities of such substances as preformed bacterial toxins and various preservatives, as phenol and tricresol, contained in the injected material.

The intradermal test has proven the most delicate means of eliciting a local anaphylactic response, but is also more likely to yield the nonspecific and traumatic reactions.

THE MECHANISM OF THE SPECIFIC ANAPHYLACTIC SKIN REACTION.

While the symptoms and lesions of general anaphylaxis as manifested in man and the lower animals are fairly well understood, the mechanism of the phenomenon can not be regarded as definitely established, and this is particularly recognized when an attempt is made to correlate the results of an enormous amount of research work in formulating an explanation of the mechanism of the cutaneous anaphylactic reaction.

Furthermore, an acceptable explanation of the mechanism of cutaneous anaphylaxis must include those truly wonderful urticariallike reactions which follow within a few minutes the application of a very minute dose of anaphylactogen to an abrasion of the skin, as in those exceptional cases of bronchial asthma and extreme hypersensitiveness to horse or other animal protein, and in hay fever to the protein of various pollens. One of my colleagues who is hypersensitive to the protein of the rabbit, guinea-pig, and horse and who suffers with acute asthma when brought in contact with these animals, yields an immediate typical reaction on the skin when the sera of these animals are applied to abrasions, and indeed to the application of a salt solution extract of lint through which he has inspired for 15 minutes the air of a room in which a few of these animals are kept. Similar and more familiar examples of extreme hypersensitiveness to a protein and the infinitesimal amounts which may produce an anaphylactic reaction are to be found in the attacks of hay fever due to the inhalation of air and dust carrying the particular pollen. An acceptable explanation of the mechanism of cutaneous anaphylaxis must, therefore, include these immediate reactions to very small doses of anaphylactogen as well as those reactions which follow some hours, and indeed days, after the intracutaneous or subcutaneous injection of much larger doses of protein.

In the first place, are we justified in assuming that the mechanism of general anaphylaxis and cutaneous anaphylaxis are identical? This has been the subject of considerable research over a period of several years in attempts to transfer the specific antibody in animals yielding positive skin reactions to normal animals; by testing animals sensitized at the same time and in the same manner by the skin test and others by the intravenous injection of the intoxicating dose of protein; and by first applying the skin test and after 24 hours injecting the same animals intravenously. The majority of these experiments were conducted with tuberculins and with divergent results and interpretations, but there appears to be sufficient evidence at hand to indicate that a local skin reaction may be an expression of an anaphylactic state to a certain protein, and this is accepted as established in this discussion, although there is not sufficient data at hand proving that the mechanism of the local or skin anaphylactic reaction is identical with that of the general and fatal reaction following intravenous injection.

At the present time two main theories on the mechanism of anaphlaxis are prominently before us, namely, the humoral or chemical theory which maintains that the lesions and symptoms of anaphylaxis are due to a poison derived from a protein matrix through the interaction of anaphylactogen and its antibody or a ferment in the blood and variously designated proteotoxin, anaphylatoxin, and serotoxin, and the physical or cellular theory which denies the formation and activity of this protein poison and maintains that the anaphylactogen unites with its antibody in the cell and that this union results in a disturbance causing shock of the cell.

The two schools agree at least in two points, namely, that an antibody is concerned in the phenomenon of anaphylaxis and that the anaphylactogen is always of a protein nature. Neither have very clear conceptions of the nature and mechanism of action of the antibody. While the adherents of the cellular theory maintain that the foreign protein constitutes the anaphylactogen, the adherents of the chemical theory are divided in their opinions regarding the protein matrix, some regarding the matrix as the foreign protein and others that it is the protein of the patient's own serum.

The older conception of the antibody, that held by Friedberger and widely accepted to-day, is to the effect that it belongs to Ehrlich's group of amboceptors or lytic antibodies of the third order. As is well known, an antibody of this nature, according to Ehrlich's theory, is produced through the influence of the antigen (bacteria, serum, egg albumin, pollens, etc.) upon body cells and is specific for the antigen in so far that it will unite only with its antigen and prepare the latter for the disrupting, digesting, or lytic action of a fermentlike substance normally present in the blood and called complement. In this manner the antibody producing the protein poison of anaphylaxis has the same structure and acts in the same manner as other well-known antibodies of this order, namely, the hemolysins and bacteriolysins.

According to this view we must concede that complement plays a rôle, indeed a most important one, in the production of anaphylaxis. While complement has properties suggestive of a proteolytic ferment, we know little or nothing of its true nature beyond that it is regarded as essential for the cleavage of the antigenic molecule. Sleeswijk (1), Friedberger and Hartoch (2), Loeffler (3), and others have shown that complement is diminished during anaphylactic shock; likewise Friedberger (4), making use of the observations of Nolf (5) and Hektoen (6) to the effect that complement is not bound by antigen and antibody in the presence of hypertonic salt solution, devised experiments which appeared definitely to establish the rôle of complement in the production of a protein poison and in the mechanism of anaphylaxis.

Test-tube experiments, and particularly efforts to explain anaphylaxis on the basis of the Abderhalden theory and technic, seriously question the rôle of complement in the mechanism of anaphylaxis. Williams and Pearce (7),[1] Lange (8), Jobling,

[1] Figures in parentheses, used as references, refer to publications bearing identical numbers under the head of "Bibliography," at the end of this paper.

Eggstein, and Petersen (9), and Kolmer and Williams (10) found that digestion occurred with activated serum, but to a lesser degree than results with active serum; on the other hand Stephen (11), Hauptmann (12), Bettencourt and Menezes (13), and Steisung (14) believe that a complement plays a very important rôle in Abderhalden's test. Abderhalden, himself, while believing that serum complement plays some part in the mechanism of his reaction, but in a different manner than in hemolysis or other cytolytic reactions, offers no adequate explanation of its relation to these processes.

It would appear, therefore, that if we attempt to explain anaphylactic reactions, either general or local, by an application of the well-known theory of antigen-amboceptor-complement production of the anaphylactic poison on the basis of experiments in vitro, we must prepare ourselves to believe that the actual lytic or digestive body in the serum (call it complement or true enzyme) exists in both a themolabile and themostabile condition. While hemolysis, bacteriolysis, and other cytolytic reactions will occur only in the presence of fresh complement serum, the protein poison of anaphylaxis may be produced apparently by both active or inactivated serum; otherwise it would appear that an explanation of the mechanism concerned in the production of anaphylatoxin must be withdrawn from the field of amboceptor-antigen complement activity as understood at present.

Vaughan has always called the antibody in the serum concerned in the mechanism of anaphylaxis a "ferment"; likewise Abderhalden and Jobling and Petersen have used this term. As far as I know, these observers have not clearly defined the meaning of the term "ferment" and established its relation or lack of relation to the amboceptors of Ehrlich or sensitizers of Bordet; apparently they regard the "ferment" as a proteolytic enzyme or protease. This conception of the enzyme nature of the "ferment" would correspond somewhat with the nonspecific alexin of Bordet or Ehrlich's complement and fail to harmonize with the specific nature of anaphylaxis. Otherwise it s necessary to believe that the entrance of a foreign protein calls forth the production of a specific proteolytic enzyme or ferment capable in itself of attacking and disrupting a protein matrix, and, as stated above, place the mechanism of anaphylaxis out of the realm of amboceptors and complements according to the theories of Ehrlich and Bordet.

The trend of more recent work in the mechanism of anaphylaxis by Jobling and Petersen (15) is in this direction. These investigators have produced the protein poison in vitro by chemical methods in such manner as to apparently rule out the influence of the thermolabile and easily destroyed complement or alexin; according to their views serum complement and normal proteolytic ferments are not identical and that while the former may be inactivated by heating at 56° C. for half an hour, the latter are more resistant, the increased digestive power observed following the addition of serum complement to inactivated pregnancy serum ascribed to the amounts of nonspecific protease thereby added.

It is clear, therefore, that in the humoral or chemical theory of anaphylaxis the true nature of the antibody is unknown and in dispute; Friedberger (16) was among the first to maintain that the antibody is identical with precipitin. More recently, Lake, Osborne, and Wells (17), Doerr, and particularly Weil (18), the latter being an ardent advocate of the cellular theory of anaphylaxis, are inclined to the same view without, however, offering a clear explanation of its action in vivo in the mechanism of anaphylaxis. While the rôle of precipitins themselves appear to have been excluded as directly participating in the production of anaphylactic shock, recent experiments by Zinsser (19) and others would tend to show that a precipitin possesses the nature of a protein sensitizer or antibody that sensitizes or prepares the protein antigen for lysis or destruction.

As previously stated, the chemical and cellular theories of anaphylaxis agree that the anaphylactogen is always a protein. In the cellular theory the anaphylactogen is regarded as specific, and this is in accord with accepted facts regarding the high

specificity of the anaphylactic reaction; in the chemical theory, however, there is no agreement, some maintaining that the anaphylatoxin is derived from the foreign poison or anaphylactogen and others that it is derived from the protein of the patient's own serum.

The first view held in the chemical theory is that in the anaphylactic reaction the antibody acts upon its protein antigen in a specific manner and produces in the reaction the protein poison or anaphylatoxin responsible for the lesions and symptoms of the anaphylactic reaction. For example, during an infection with spirocheta pallida an antibody is produced which, acting upon an emulsion of dead spirochetes (luetin) injected into the skin, splits the protein of these parasites in a specific manner with the production of a poison responsible for the local reactions of erythema and infiltration.

An anaphylactic reaction of this kind employing a cellular or formed antigen is regarded as being divided into twophases. As compact structures cells can not enter into direct chemical relations with the fixed tissue cells until they have been resolved or disintegrated into simpler constituents by ferments or antibodies in the body fluids. This is followed by the second phase or the interaction of the anaphylactic antibody and the dissolved antigen. Anaphylactic reactions with such formed elements as erythrocytes and bacteria may occur; usually it is more difficult to sensitize the body cells with these antigens than when dissolved proteins as in blood serum are employed.

The experiments of Keysser and Wassermann (20), Bordet (21), Jobling and Petersen (22), Plaut (23), Peiper (24), Freidemann and Schonfeld (25), Bronfenbrenner (26), and others tend to show that the mechanism is not quite so simple and direct and that a protein poison may be produced in the absence of the specific antigen. They have demonstrated by experiments in vitro that such inert substances as kaolin, barium sulphate, agar or indifferent bacteria or precipitates may replace the antigen in the production of a protein poison. Since the presence of protein substances could be excluded as with such inorganic substances as kaolin and barium sulphate, the conclusion was naturally drawn that the matrix of the poison was not the antigen or subtract, but the constituents of the serum itself. Jobling and Petersen advanced the theory that the proteolytic ferment was held in check by antiferments (largely the unsaturated fatty acids in serum) and that these substances as kaolin or barium sulphate absorb the antiferments and thereby release the proteolytic ferments which proceed to digest the protein of the serum. For this reason these investigators have applied the name "serotoxin" to the protein poison as indicating its source.

Applying these observations and views to the subject under discussion, it would appear necessary to infer that the antigen is nonspecific and acts as it were in a purely mechanical manner; this does not at all agree with great mass of experimental data showing the highly specific nature of anaphylaxis. In tertiary syphilis, for example, the reaction in the skin following an injection of an emulsion of dead spirochetes (luetin) would be due according to this mechanism, not to a digestion of the protein of the spirochetes with the production of a protein poison, but the luetin would act simply as a local adsorbent of the antiferment, releasing thereby proteolytic ferments which proceed to digest the patient's own serum or cellular protein in loco with the production of a poison responsible for the reaction, and if this were true the reaction lacks specificity.

Bronfenbrenner (27) explains the specific production of anaphylatoxin by nonspecific ferments or antibodies as follows:

Specific antibodies are produced which, combining with the antigen, causes a falling out or inactivation of the antiferments of the serum by a change in colloidal conditions resulting in the release of normal or nonspecific proteolytic ferments which disrupt or digest the protein of the serum. In other words, specific antibodies are produced, but instead of these digesting the protein of the antigen or of the serum directly, they act by uniting with the antigen, and this union results in the removal of antienzyme,

thereby releasing or rendering active the normal and nonspecific enzymes of the serum which produce a protein poison or anaphylatoxin by digesting the protein of the serum.

Whether or not the results of a study of the mechanism of Abderhalden's reaction, which in the final analysis is nothing more than a popularized method of studying protein digestion in a manner pregnant with opportunities for error, can be applied to unfolding the mechanism of anaphylaxis is uncertain; but it is certain that an explanation of the mechanism of either the local skin or general anaphylactic reaction must satisfactorily explain the high and uniform specificity of these reactions before it is acceptable.

The above-mentioned experiments which have been largely conducted in vitro are not without definite value, and, as I shall point out later, have a greater bearing upon the mechanism of the pseudo than upon the true anaphylactic reaction and the phenomena of local inflammation in general.

Up to this point our discussion has been confined to present-day conceptions of the nature of the protein matrix, the mechanism of action of the antibody or ferment according to the chemical theory and the effects of the protein poison on body cells in anaphylactic phenomena.

No discussion is complete, however, without particular reference to that peculiar change on the part of the cells, probably involving the colloidal chemistry of the cells themselves, which exerts so important a rôle in anaphylaxis and particularly in the local reaction. This altered reactivity of the cells or their unusual and exaggerated susceptibility to the effects of the products of digestion of foreign proteins was early emphasized by Von Pirquet, Rosenau, and Anderson, and other pioneers in this field, and on account of the importance of this phase, the former proposed the term "allergy" meaning "altered reactivity," as describing the phenomena more concisely than Richet's term "anaphylaxis," meaning "without protection." The term "allergy" is, in our opinion, more appropriate, as it emphasizes the important hypersensitiveness or altered reactivity of the cells regardless of any theories we may entertain as to the manner in which this change is brought about or manifested.

Definite information on the nature of this peculiar cellular change is lacking. When one bears in mind the intense local, focal, and general reaction in tuberculosis that may follow the injection of a minute amount of tuberculin or the minute amount of protein that suffices to induce the anaphylactic reaction in the classical experiment with horse serum and guinea pigs, conditions in which the amount of protein poison produced must be very slight indeed for physical reasons alone, the supposition is forced upon one that some change rendering the cells highly susceptible to the anaphylactic poison is of fundamental importance in anaphylactic reactions.

Investigators have attempted to explain this peculiar hyperactivity of the body cells on the basis that the reaction is a cellular one, that is, that the antibody is within the cell and that the antigen-antibody reaction occurs in this position rather than in the blood stream by means of free or circulating antibody and antigen. According to the "cellular theory," if the serum of an immunized animal containing the anaphylactic antibody is injected into a normal animal (passive anaphylaxis) followed by an injection of the antigen, an anaphylactic reaction can not occur before the elapse of sufficient time for the antibody to become anchored to cells. According to the "humoral theory," on the other hand, the antigen meets the antibody in the blood stream and explains the time required between the injection of immune serum and antigen in passive anaphylaxis as due to a failure of rapid union between antigen and antibody unless quantitative relations between the two is accidentally correct.

The early theory of Friedberger (16) explaining anaphylaxis on the basis of "sessile receptors;" the experiments of Friedberger and Girgolaff (28), who passively sensitized normal animals by transplanting the thoroughly washed organs of a sensitized animal; the transfusion experiments of Pearce and Eisenbrey (29), who transferred

the blood of a sensitized animal to a normal animal and the blood of a normal animal to a sensitized one, finding that the latter, but not the former, reacted when the antigen was injected as soon as the transfusions were completed; the work of Coca (30) who found that sensitized guinea pigs would still react after being thoroughly bled and perfused with salt solution; of the investigations of Schultz (31), Dale (32), and particularly of Weil (33), showing that the excised and washed muscles of sensitized animals would react in vitro in a bath of Ringer's solution when the antigen was added, support most strongly the cellular theory of anaphylaxis as emphasized also in the work and recent communications of Doerr (34).

In the opinion of Weil, Doerr, Bayliss, Coca, and others the "cellular" theory is the only tenable one to-day. According to this theory of anaphylaxis the antibody is in or on the body cells; upon union with the antigen the cells undergo a physical shock which has been likened to an electrical shock, and this constitutes the basis of the anaphylactic reaction without the formation of any intermediate or chemical poison.

As emphasized by Weil (36), there is no direct evidence of the production of a chemical poison or anaphylatoxin during or after an anaphylactic reaction in the living animal. This poison has not been satisfactorily demonstrated in the blood and in animals recovering from a general anaphylactic reaction, the phenomena being more suggestive of a transitory "shock" than an intoxication with a chemical poison.

On the other hand the mass of experimental evidence indicating that the anaphylactic reaction is not purely cellular, but at least in part an intravascular reaction, is too strong to be discarded. As pointed out by Zinsser and Young (35), the necessary time usually required in passive anaphylaxis between the injection of immune serum and antigen may be due to slow union between antigen and antibody in the blood stream on the basis that the anaphylactic reaction involves the interaction of colloids, and that a protective colloid is responsible for the slow union of antigen and antibody unless its influence is obviated by exact quantitative proportions between antigen and antibody, which under experimental conditions may be secured in a more or less accidental manner.

As antibodies are produced by the body cells, it is reasonable to believe that they are present in the protoplasm of the cells, and even after thorough washing of the tissues are capable of union with their antigen. It is entirely likely that these attached or sessile antibodies are chiefly concerned in the phenomena of anaphylaxis, but I can not subscribe entirely to the cellular theory because of the mass of experimental data bearing on the production of the protein poison, particularly in vitro, by the free antibodies in an immune serum. The reactions in vivo of hemolysis and bacteriolysis which are lytic processes apparently similar to those concerned in anaphylactic reactions are probably intravascular processes; it is also likely that in anaphylaxis to formed antigens the first phase of the reaction, that is, the disruption of the antigenic cell, is intravascular, showing that lytic reactions entirely analogous to our conception of the mechanism of the production of the protein poison in anaphylactic reactions may occur in the blood stream. For these reasons alone I can not exclude the free antibodies in the blood from playing some role in the phenomena of anaphylaxis.

The extreme sensitiveness of the body cells in anaphylaxis to the protein suggests to me that the cells acquire the property of union with the protein poison to an extreme degree, as if they were furnished as a result of the initial dose of foreign protein, with an increased number of specific and sessile receptors for the protein poison. In other words, while the protein poison may be produced in the cells by sessile receptors or in the blood stream by free receptors, anaphylaxis itself, that is, the hypersensitiveness of the cells is due to the increased binding power of the cells for the protein poison. In our opinion this in part explains true allergy, that is, the effects of local or general sensitization (production in the protoplasm of the cells of increased receptors for the

protein poison) and the immediate well marked or even violent effects following the production of what must be very minute amounts of protein poison as in the cutaneous tuberculin reaction or in the classical horse serum reaction in guinea pigs following the intravenous injection of the intoxicating or second dose of protein in every minute or infinitesimal dosage.

Personally I would be more prepared to understand and accept the cellular theory in the strictest sense in the mechanism of anaphylaxis were my studies confined entirely to general anaphylactic shock; in the local reaction, however, the slowly spreading character of the lesion, the erythema, edema, and eosinophilic infiltration strongly suggest that a diffusible irritant has been produced similar in some respects at least to that which can be produced in vitro.

As far as I am aware the skin or local anaphylactic reaction has not been explained on the basis of the cellular theory alone in its strictest sense. These reactions have many of the features on an inflammatory reaction of which vascular changes (hyperemia) and edema are prominent features. Intracutaneous reactions are likely to persist for several days; likewise the cutaneous tuberculin reaction, although the cutaneous reaction to pollen and serum may reach its height within half an hour and disappear within a few hours. May these inflammatorylike changes be ascribed to a temporary and physical shock of the endothelium of vessels in the skin followed by stasis and exudation, and of the connective tissue cells at the site of injection? As previously stated, I believe that the cells play the major role in anaphylaxis in that the formation of a diffusible protein poison occurs largely in or on the cells by reason of the fact that the antibodes are largely situated in the cells and that the cells bear the brunt of the change and undergo shock by reason of the poison being produced in them, but that a poison, nevertheless, is produced which may escape detection by high dilution in the body fluids in the general reaction, but which appears in the local reaction as a diffusible irritant producing the phenomena of acute congestion, edema, and leucocytic infiltration (particularly of eosinophiles).

It is my opinion that the source of the protein poison in true anaphylaxis is always that which has been injected and for which specific antibodies are present mainly in the cells.

I regard cutaneous anaphylaxis as due to an interaction between true or specific antigen and its specific antibody with the production of a diffusible irritant capable of exciting inflammation; that this union of antigen and antibody occurs principally within the cells and that the cells suffer largely by reason of this interaction and formation or irritant within them.

An adequate explanation of those apparently anaphylactic reactions to drugs has not been made. It is generally held that the drug alters a body protein with the formation of a new protein compound capable of sensitizing and producing anaphylaxis. Recently my colleague, Dr. Fred Boerner, who is hypersensitive to quinine and suffers considerably with cutaneous manifestations if even minute doses are swallowed, has shown a marked reaction of edema and erythema in his skin following in few minutes the application of powdered quinine sulphate or a solution of the bisulphate, to an abrasion. He has shown that this reaction is apparently specific inasmuch as it does not occur among persons not hypersensitive to quinine and a similar reaction occurred in the skin of a second person known to be hypersensitive. The occurrence of these reactions within a few minutes after the application of quinine renders the theory of the formation and activity of a new protein compound doubtful.

MECHANISM OF NONSPECIFIC PROTEIN AND TRAUMATIC SKIN REACTIONS.

It appears well established that the blood serum, leucocytes, and the fixed cells of various tissues of the body contain proteolytic ferments capable of digesting various protein substances in vitro. The digestive activity of these ferments can be studied and determined only by very delicate methods and are apparently nonspecific in

character (37). In vitro they apparently are capable of producing toxic substances which may be regarded as protein derivatives. These proteolytic ferments may be responsible for local inflammatory phenomena and in an attempt to corelate these results with the mechanism of the nonspecific and purely inflammatory reaction which may be the sole reaction in the skin and lead to misinterpretation and error, or, occur coincidently with the true anaphylactic reaction, the following explanations have been offered:

1. An irritant is produced through the interaction of general proteolytic ferments and various proteins injected, as those contained in broth, agar, or ascites This irritant or chemical poison is responsible for the lesion.

2. Trauma caused by the needle or trauma plus injury to the cells due to the presence of a preservative, as phenol or tricresol, or a preformed toxin (as diphtheria toxin used in the Schick test), or bacterial protein of irritant nature, may destroy a sufficient number of cells to release their proteolytic ferments which proceed with a process of digestion; or the injection mass and dead cells mechanically absorb the antiferment and thereby activate the ferments which produce from the injected protein or that of the dead cells and patient's own serum sufficient proteotoxin to produce an inflammatory reaction.

The injection into the skin of a foreign protein (the anaphylactogen), as that protein present in sterile bouillon or, for example, the protein of bouillon, agar, and spirochetes as present in luetin, increases the production of protein poison by more active release or proteolytic ferments through removal of the antiferments by absorption or in some other way, followed by digestion of the injected protein and the protein of the patient's devitalized cells and serum.

This protein poison or proteotoxin is an irritant and excites inflammation of varying degrees of severity. In this manner we have a ready explanation for those pseudo reactions following the intracutaneous injection of sterile broth as found by Kolmer and Moshage (38), of extracts of placental cells by Engelhorn and Wintz (39), Falls and Bartlett (40), Kolmer and Williams (41), of agar and emulsions of normal and pathologic skin by Stokes (42, 43), of heated diphtheria toxin-broth by Zingher (44), and various other protein substances by various investigators.

It is highly probable that the quantity of proteolytic ferments in the cells and serum of different persons vary; also the quantity of ferments in the cells of the skin of the same person in different areas of the body, and in this manner explain the varying degrees of pseudo or purely inflammatory reactions in the same person in different parts of the body or among different persons, with the injection of the same protein in the same dosage. Dr. Moshage and I have found that the skins of persons convalescent from scarlet fever and measles are especially prone to yield these nonspecific reactions.

Any protein substance, if injected into the skin in sufficiently large amount, will elicit a nonspecific or inflammatory reaction; for this reason the material used in conducting skin tests for the specific anaphylactic reaction should be carefully prepared and administered in such amount as will not elicit a nonspecific reaction among a large number of controls, and the injection of a control fluid is always advisable. Cutaneous tests are much less likely than intracutaneous tests to yield nonspecific reactions of sufficient degree to prove disturbing; they are less delicate tests for the anaphylactic state but also less open to error.

THE INFLUENCE OF DRUGS UPON SKIN REACTIONS.

Recently Sherrick (49) has reported that normal persons under the influence of iodides would yield positive reactions to the intracutaneous injection of luetin. Broadwell, Matsunami, and I (50) were able to confirm these observations in that a normal person who reacted negatively to luetin in the preliminary test would frequently react to a well-marked degree when the test was applied after the admin-

istration of potassium iodide. We also observed similar results among rabbits and guinea pigs.

During the past year these studies have been continued with the cooperation of Dr. Immerman and Dr. Montgomery (51), using various iodides, bromides, chlorides, and anesthetics and two intracutaneous tests, namely, the luetin test and one with an emulsion of B. prodigiosis. Both tests were made beforehand upon Wassermann negative persons and repeated after the administration of from 90 to 170 grains of the drugs or after operation under ether or nitrous oxide. Iodides and bromides were found to exert considerable influence, while the influence of chlorides was much less in evidence, and ether and nitrous oxide were without demonstrable effect.

According to Jobling and Petersen, the antiferment of the serum is of the nature of unsaturated fatty acids and that these may be removed by the halogens and the ferments thereby released or rendered active. The influence of these drugs upon skin tests are, therefore, to be explained upon this basis. We are of the opinion that they do not influence the mechanism of the true anaphylactic reaction, but only the nonspecific or simple inflammatory portion of a skin reaction by facilitating the release of nonspecific ferments. This opinion is based upon the observation that the influence of these drugs upon skin reactions have been observed in persons who were not anaphylactic to the protein; that no influence was observed upon true anaphylactic reactions to the cutaneous application of tuberculin and that the greater the amount of bacterial protein or culture medium constituents injected, the severer the reaction.

Since the nonspecific element may always play a part in skin reactions following intradermal injections, it is well for physicians to bear in mind that these drugs may so favor the nonspecific reaction as to present evidences of a violent reaction which may be interpreted as anaphylactic.

THE CLINICAL SIGNIFICANCE OF ANAPHYLACTIC SKIN REACTIONS.

1. *As indices of hypersusceptibility and infection.*—The clinical significance of a true anaphylactic skin reaction to a certain protein aside from establishing the fact that a person is hypersensitive to that protein, depends upon what harm may be done with the enteral or parenteral introduction of the protein. It is not my purpose to review in detail the many clinical conditions which appear to be due to a state of anaphylaxis; this phase of the subject has been recently covered in a thorough and excellent manner by Longcope (52). Here it may be recalled that examples of apparently true spontaneous hypersensitiveness to various foreign proteins are not uncommon and indeed, the trend of recent investigations is always widening this field and establishing hypersensitiveness as a probable basis for many diseases with symptoms referable to the respiratory tract, gastro-intestinal tract, and the skin. In the minds of not a few physicians the term "anaphylaxis" means a brief and stormy general reaction following the administration of diphtheric antitoxic horse serum, a reaction occupying as it were a distinct and isolated place in the field of immunity, whereas this is but one manifestation of a process which bids fair to become established as the basis of many and diverse clinical conditions, as, for examples, hay fever, ivy poisoning and similar toxic dermatoses, bronchial asthma, serum sickness and that wide field of various food idiosyncrasies due to the ingestion of eggs, milk, and various meats as studied by Schloss (53), Lesné and Richet (54), Talbot (55), Smith (56), Strickler (57), Blackfan (58), and others. I have been particularly interested in the investigations conducted in my laboratory by Strickler, which show the very important relation of hypersensitiveness to various vegetable and animal proteins to eczema and other skin diseases.

Further researches will show us what harm may be done by the anaphylactic poison; at present we know that grave symptoms and even death may result from the paren-

teral injection of a serum to which a person is highly susceptible; Longcope and his coworkers have shown that the poison may produce slow but definite degenerative lesions in the kidneys; the ingestion of eggs or other food by a person hypersusceptible to their protein is known to produce symptoms and skin manifestations which disappear or ameliorate upon the permanent withdrawal from the diet of such foods. In other words evidence is accumulating to show that hypersensitiveness plays an active rôle in the etiology of many diseases and in the detection of these, skin reactions are proving of great value and indeed may prove the only means of specific diagnosis.

As is well known, anaphylactic skin reactions may be elicited in various bacterial and protozoon diseases with anaphylactogens prepared of the protein of the respective microparasites particularly in tuberculosis, glanders, typhoid fever, and syphilis. Well-marked and specific reactions have also been found by Amberg (59) and Kolmer and Strickler in ringworm and favus and isolated reports show that they may be elicited in various other diseases with the proper preparations.

In these conditions, however, the skin reactions are not always elicited and especially during the early and acute stages. An interval of time is required for the purpose of sensitization and during the acute stages antigen and antibody may both be present in the cells and body fluids as shown by Weil (60) and Denzer (61) with continual interaction expressed in the symptom complex of the infection and thereby giving no response when the protein is applied or injected into the skin. Furthermore the chemical nature of the protein of our anaphylactogen may have been altered in the course of preparation to a sufficient extent to fail to elicit an anaphylactic reaction. These and other factors not understood diminish the practical value of a skin test. At present, however, it may be stated that they possess a diagnostic value which is particularly high in chronic infections and that no other satisfactory clinical or laboratory test for the state of anaphylaxis to a particular protein and for the anaphylactic antibody, has been discovered except that by which the protein is actually brought into relation with the body cells as in the parenteral introduction of the protein. Of great interest in this connection is the relation of the intensity of the anaphylactic skin reaction to the extent of the infection. Krause (66) has recently studied in a thorough and excellent manner the tuberculin skin reaction in relation to experimental tuberculosis, finding that cutaneous hypersensitiveness to tuberculoprotein is inaugurated by the establishment of infection and the development of the initial focus; that the skin reaction increases with progressive disease; is diminished with healing and increased by reinfection.

2. *As indices of immunity.*—Of further importance is the question of the clinical significance of a local anaphylactic reaction as an index of immunity; that is, resistance to an infection or reinfection. Is the anaphylactic antibody capable of attacking and destroying the antigenic protein in a living state? Are protective and curative antibodies produced by the defensive mechanism of the body while the cells are being sensitized and the anaphylactic antibody produced? In other words is hypersensitiveness to be regarded as an index of resistance?

In 1798 Jenner wrote:

> It is remarkable that variolous matter, when the system is disposed to reject it, should excite inflammation on the part to which it is applied more speedily than when it produces the smallpox. Indeed, it becomes almost a criterion by which we can determine whether the infection will be received or not.

In other words, as previously mentioned, this astute observer noted that a person who presented within a few days at the site of vaccination an "efflorescence of palish color" was probably immune to smallpox. Force (62) has recently drawn attention to this "immediate" reaction to inoculation with cowpox virus as an evidence of resistance or immunity to cowpox and smallpox and my own experience supports his conclusions. Here, indeed, we have evidence at hand indicating that an anaphylactic state is an index of the coincident presence of antibodies and resistance.

Investigations bearing upon the relation of anaphylaxis to immunity in other infections have not generally yielded these results. Rosenau and Anderson (63) sensitized pigs with extracts of B. typhosus and B. coli and found that animals so treated were immune to amounts of the respective microorganisms fatal to normal pigs; Romer (64) and Sata (65) in experiments among cattle with B. tuberculosis reached the conclusion that a state of hypersensitiveness meant a certain degree of resistance while Krause (66) and Austrian (67) have expressed the opinion based upon experiments, that sensitization of nontuberculous animals with tubercle protein does not raise their resistance to experimental tuberculosis infection and indeed may lower it.

More recently Gay and Force (68) have greatly renewed interest in this subject by advocating the skin test as a means of determining defensive activity following typhoid fever or active immunization by means of vaccines. Their first work was conducted with a "typhoidin" prepared in the same manner as Koch's old tuberculin, by cutaneous inoculation; later Gay and Claypole (69) prepared typhoidin by precipitating the solution with alcohol, washing the precipitate with alcohol and ether, drying in a vacuum and suspending the resulting powder in phenolized normal salt solution which was injected intracutaneously and applied cutaneously; a control powder was prepared from broth and used in the same manner. With this skin test Gay and his associates have studied the relative value of various vaccines and regard the anaphylactic reaction as indicative of a state of immunity. Nichols (70) has questioned the value of the anaphylactic skin test as an index of ammunity and regards the typhoidin reaction as indicating nothing more than sensitization of typhoid protein which is apparently less lasting and less specific than the true immunity to this infection. He bases this opinion on the fact that in his experience the typhoidin skin gave fewer positive reactions (75 per cent) than generally expected, as about 90 per cent of persons who have had typhoid fever are immune for many years or even for the balance of life. Furthermore, according to Nichols, experience has shown that protection following typhoid fever is of longer duration than is indicated by the typhoidin test and while a large percentage of persons who have had typhoid fever or have been immunized with typhoid vaccine react to paratyphoidin recent experiences and statistics particularly in Europe have indicated that these persons are not immune to paratyphoid fever.

My own experiments in this field have been largely tests in vitro for various antibodies as agglutinins, bacteriolysins, and complement-fixing substances in the fresh sterile blood sera of persons hypersensitive to various proteins in order to determine whether or not the state of hypersensitiveness to a particular bacterial protein was accompanied by demonstrable amounts of these antibodies. I am well aware of the shortcomings of such tests and that the weight of opinion minimizes their value as an index of actual immunity. As previously mentioned, Friedberger (16) was among the first to maintain the identity of precipitin and the anaphylactic antibody; Doerr and Russ (71) independently reached the same conclusion and more recently Lake, Osborne, and Wells (17) and Weil (18) have brought forward considerable evidence in support of the view that percipitins are frequently persent in the serum of the sensitized animal.

The experiments conducted by Mr. Berge and the author (72) with reference to the typhoidin skin reaction showed that while the bactericidal power of human serum over B. typhosus is increased in a proportion of persons following typhoid fever or active immunization with a vaccine, there is no direct relation between the typhoidin skin reaction and the results of bactericidal tests in vitro. Likewise no definite relation was observed between the presence of agglutinins and complement-fixing antibodies and the skin reactions.

A similar study in syphilis by Broadwell and the author (73) has shown that in human syphilis spirocheticidal antibodies for culture pallida are practically absent from the

sera of those persons who do and who do not react to the intracutaneous injection of luetin. Likewise no constant relationship was found between the occurrence of cutaneous hypersensitiveness to luetin and the presence of agglutinins for culture of pallida and of a complement-fixing antibody with an antigen of luetin.

Similar studies in diphtheria by the author (74) likewise showed an absence of any relationship between cutaneous hypersensitiveness to a polyvalent and detoxized emulsion of diphtheria bacilli or diphtherin (75) and the presence of such antibodies as antitoxin, agglutinin, bacteriolysin, and complement-fixing substances for diphtheria bacilli.

Additional studies by Harkins, Matsunami, and the author (76) along the same lines in canine distemper have shown that the sera of dogs reacting positively to the intracutaneous injection of a polyvalent emulsion of B. bronchisepticus (77) do not show the presence of agglutinins, bacteriolysins, and complement-fixing antibodies for this bacillus in any constant relationship to the skin reactions.

In a strict sense the question whether or not an anaphylactic skin reaction may be taken as an index of defensive activity can only be answered on the basis of actual protective experiments. Time alone will tell whether or not the person presenting a positive reaction to typhoidin is actually immune to typhoid fever as claimed by Gay and his associates. Experiments among rabbits with cultures of spirocheta pallida by Noguchi (78) consisting in the immunization of the animals until they reacted to the intracutaneous injection of luetin followed by an actual test of their immunity to living virulent spirochetes by inoculating the testicle have given Dr. Noguchi the impression that the immunization reduced susceptibility in some rabbits while it had no effect whatsoever in others and indeed seemed to render some more susceptible. Furthermore, it is highly probable that the syphilitic is open to reinfection with spirocheta pallida; certainly our experiments failed to show the least evidence of spirocheticidal antibodies in the sera of tertiary sylphilitics reacting positively or negatively to the intracutaneous injection of luetin, and it is highly probable that the luetin reaction does not indicate resistance to reinfection on the "lighting up" of a present infection.

Furthermore, I have seen three persons presenting perfectly typical reactions to diphtherin contract diphtheria and dogs which have reacted to bronchisepticin have contracted canine distemper.

The sum total of these studies indicate that while antibodies which may be regarded as possessing protective and curative properties toward a certain protein may be present in the body fluids of persons and animals hypersensitive to this particular protein, the condition of hypersensitiveness in itself is no direct evidence of their presence or of resistance to a particular infection, although these antibodies are most likely to be present in the body fluids of those persons who are hypersensitive. The positive anaphylactic skin test is therefore evidence of infection or sensitization to a particular protein without bearing any direct relation to resistance to infection or reinfection.

The clinical significance and practical value of skin reactions are largely of a diagnostic nature for the detection of hypersensitiveness to a protein or proteins which may when introduced into the organism produce various acute or chronic lesions and symptoms of disease.

CLINICAL SIGNIFICANCE OF THE PSEUDO OR NONSPECIFIC PROTEIN AND TRAUMATIC SKIN REACTIONS.

At the present time the chief clinical significance of the pseudo anaphylactic and traumatic skin reactions is the likelihood of mistaking them for true anaphylactic reactions.

The Schick toxin test for immunity in diphtheria is regarded at present as due to the direct irritant action of diphtheria toxin upon cells at the site of injection; if

antitoxin is present in sufficient amount the toxin is neutralized and the inflammatory reaction does not occur. Trauma alone, the preservative, the interaction between protein constituents of the broth and nonspecific ferments or between the protein of autolyzed diphtheria bacilli and specific ferments, may induce a pseudo reaction which may be mistaken for the true reaction.

It is probable that certain conditions accompanied by an increase of cells and their destruction as in cancer and pregnancy may result in the temporary increase of nonspecific proteolytic ferments in body fluids and cells and increase the tendency for the production of pseudo reactions in the skin; as previously stated there is also reason to believe that certain diseases accompanied by skin manifestations as scarlet fever and other exanthemata, increase the tendency to skin reactions.

SUMMARY.

1. Skin reactions may be (1) true or specific anaphylactic reactions; (2) pseudo or nonspecific protein reactions, and (3) traumatic reactions.

2. A nonspecific or traumatic skin reaction may occur coincidently with, or be mistaken for, a true anaphylactic reaction.

3. Intracutaneous skin tests are more delicate than cutaneous tests, but also more likely to yield the nonspecific and traumatic reactions.

4. The traumatic and nonspecific protein skin reactions may be caused (1) by trauma and the direct injection of an irritant used as a preservative for the material, as phenol, or, to a performed toxic and irritant substance, as diphtheria toxin in the Schick test; (2) to the production of a protein poison of irritant qualities by the action of nonspecific proteolytic ferments in the serum or derived from injured cells, upon the protein of the patient's serum, devitalized cells, injected protein, or all three.

5. The true anaphylactic skin reaction, however, is a specific process due to the interaction of specific anaphylactic antibody and specific anaphylactogen, largely within or upon the cells and with the formation of a diffusible irritant similar to that produced in the nonspecific reaction, capable of producing acute hyperemia, edema, and leucocytic infiltration of the skin.

6. Certain drugs as potassium iodide and potassium bromide increase the nonspecific reaction by facilitating the activity of nonspecific proteolytic ferments and the production of protein poison, through the removal of antiferment; these drugs probably have no direct influence upon the specific anaphylactic reaction.

7. The specific anaphylactic skin reaction is acceptable as a delicate index of hypersensitiveness to a certain foreign protein or proteins, the enteral or parenteral administration of which may be expressed by various lesions and symptoms of disease.

8. The severity of a true anathylactic skin reaction appears to be an index of the degree of hypersensitiveness.

9. A state of cutaneous anaphylaxis to a particular bacterial protein is not of itself an index of resistance or immunity to the living microparasite, although immunity principles may be coincidently present with the anaphylactic antibody.

10. At present the main clinical significance of the nonspecific protein skin reaction is the likelihood of mistaking it for a true anaphylactic reaction.

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The CHAIRMAN. The next paper is by Dr. G. H. A. Clowes on "The relation of hay fever to anaphylaxis."

THE RELATION OF HAY FEVER TO ANAPHYLAXIS, TOGETHER WITH A THEORY REGARDING THE NATURE OF ANAPHYLACTIC PHENOMENA.

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Following a method somewhat analogous to that adopted by Noon and Freeman in the treatment of the European form of hay fever, a series of experiments has been carried out in the course of the last four years on the treatment of the American or autumnal form of hay fever by vaccination with the extracts of plant pollens. The pollens employed for this purpose were first dehydrated by means of a mixture of acetone and ether and subsequently extracted with water. [1] This method is vastly superior to the freezing and thawing method previously employed by Dunbar, and Noon and Freeman, owing to its greater simplicity and the greater durability of the product obtained.

Sufferers from either the spring or autumnal variety of hay fever exhibit a sensitiveness to one or more varieties of plant pollens when tested by means of the ophthalmic or cutaneous method. In the most highly sensitized cases a flush may be produced in the eye by introducing a drop of a solution containing 1 part in 500,000 of the soluble constituents of the pollen to which the individual is sensitive. Group reactions are frequently obtained; for example, an individual sensitive to 1 part in 500,000 of ragweed may exhibit a sensitiveness to 1 in 50,000 of golden rod or other members of the Compositæ family. Similarly an individual sensitive to 1 in 500,000 of timothy may exhibit a less marked but definite sensitiveness to some other member of the Graminaceæ family, but only those unfortunate individuals who suffer from both the spring and autumnal varities of hay fever will exhibit a sensitiveness to pollens of plants belonging to both the families in question.

A marked alleviation of symptoms and reduction in sensitiveness may be effected by injecting dilute extracts of the pollens to which the individual is sensitive, at intervals of three or four days, starting with doses as small as 1 cc. of 1 in 5,000,000 and gradually increasing the dose until a maximum dose of 1 cc. of 1 in 5,000 to 10,000 is attained. If the treatment is suspended, sensitiveness develops once more, and in the course of a few months will be almost equal to that preceding treatment, but it has been found that in each successive season of treatment the symptoms of the disease become less marked, from which it may be hoped that complete cure may ultimately be effected.

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[1] Clowes, A preliminary communication on certain specific reactions exhibited by hay fever cases. Proc. Society for Experimental Biology and Medicine, 1913, pp. 69–72.

Clowes, A preliminary communication on the treatment of autumnal hay fever by vaccination with an aqueous extract of the pollen of ragweed. Ibid.

The condition is certainly not strictly analogous to anaphylaxis, as it is impossible to secure complete relief of symptoms by the use of a single desensitizing dose. The occurrence of a cutaneous reaction at any point in the body, as well as the occasional occurrence of complement deviation in the blood, indicates that the reaction is systemic and not confined purely to the mucous membranes. All attempts to induce hay-fever symptoms in normal individuals by introducing into their eyes pollen extracts which have previously been incubated with the serum of individuals sensitive to the pollen in question have failed of result. From this and other experiments to be reported later the phenomena exhibited in hay fever, asthma, etc., appear to support the conclusion that sensitization phenomena are rather attributable to disturbances in the colloidal equilibrium of certain constituents of the cell than to the production of split products as a result of peptization of antigen.

That the immune phenomena developed are specific was demonstrated by immunizing certain individuals sensitive to two widely differing pollens against one only of the varieties in question. A reduction in sensitiveness to this particular variety was noted, accompanied by a retention of the full measure of sensitiveness to the pollen against which no immunization was employed. Within a single group of closely related plants, immunization by means of one member of the group will confer a measure of immunity against other members of the same group, although possibly to a less marked extent than is obtained against the pollen of the plant specifically employed. A nonspecific immunization or, rather, reduction in sensitiveness may be effected in certain cases by administering large doses of calcium salts. It is worthy of note that well-nourished individuals appear to respond more readily to treatment with calcium salts. A marked variation in the results attained from vaccination has been noted in upward of 100 cases submitted to experiment. In 25 per cent of cases, especially those which have been treated for several years, almost complete alleviation of symptoms has been attained by means of repeated vaccination. In a further 40 per cent to 50 per cent of cases a partial alleviation of symptoms has been effected. In the remaining cases practically no results have been obtained. But it appears probable that in spite of the large variety of pollens employed those cases in which no results have been obtained owe their symptoms to causes other than those which have thus far been investigated. Support is lent to this point of view from the observation that those showing the most marked sensitiveness to a given variety of pollen are most readily treated. Sensitization to a certain variety of flies has been successfully treated by vaccination with the soluble extracts of the flies in question. An investigation of the sensitization phenomena of plants, animals, and a variety of foreign proteids indicates that the condition occurs far more frequently than is generally appreciated, and is responsible not only for hay fever and asthmatic symptoms, but also for certain gastro-intestinal and other disturbances not at present understood.

Susceptibility to the development of sensitization phenomena appears to be an inherited characteristic. In a large number of families, data regarding which has been obtained over a period of several generations, the occurrence of one or another form of sensitization follows Mendelian lines and suggests the advisability of further study in this direction. If sensitization is attributable to the passage of colloidal aggregates through the mucous membrane in a sufficient state of aggregation to induce immune reactions, it is obvious that the transmitted characteristic in question may be simply abnormally low or impaired resistance or lack of impermeability of the protoplasmic membrane.

In conclusion it is necessary to sound a note of warning against promiscuous experimentation with these extremely powerful pollen toxins. The administration of an overdose may readily produce serious anaphylactic symptoms, and the employment of mixed vaccines containing not only the pollens to which the individual is sensitive but other pollens of the same or related families, is obviously to be deprecated. The results obtained by treatment with calcium lactate suggest the possibility that ulti-

mately some better procedure than that of vaccination may be developed for counteracting the tendency to various forms of protein sensitization, which under the conditions of modern civilization appear to be increasing.

Turning now to the question of the nature of anaphylaxis. Three years ago the writer demonstrated that the antagonistic effects exerted by electrolytes in biological systems could be closely paralleled in purely physical systems and are dependent upon the relative capacity possessed by individual electrolytes or their component ions to promote or inhibit the dispersion of soap films in water as compared with an adjacent lipoid or fatty phase, or of other concentration films formed between protein and water phases, in water as compared with the protein phase. If a given volume of an aqueous solution of sodium oleate or caustic soda is allowed to flow from a capillary pipette through oil containing a certain amount of fatty acid, the number of drops produced will depend upon the strength of the solution of soap or caustic soda employed. The greater the concentration the larger the number of drops; the greater the dilution the smaller the number of drops. If NaCl is added to a system of this sort, the number of drops will be greatly increased. If $CaCl_2$ is added the number of drops will be reduced. NaCl and $CaCl_2$, when employed in those ratios in which they exert a compensatory or balancing effect upon one another in nature, exert no effect upon the number of drops produced in such a system. These results are attributable to the fact that a surface film of soap is formed at all points of contact between water and oil. Alkalies and salts of the monovalent cations, like NaCl and KCl, by increasing the dispersion of the soap film in water as compared with oil, exert a destructive effect on the film, reducing its relative resistance to the passage of water and water-soluble constituents, consequently causing a break in the film at an earlier point than in the system, with a consequent production of a larger number of drops. Acids, salts of calcium, barium, strontium, iron, and other divalent and trivalent cations exert on the other hand a protective effect, decreasing the relative dispersion of the constituents of the film in water as compared with oil, thus promoting the continuity of the film, increasing its resistance to the passage of water and water-soluble constituents with a consequent diminution in the number of drops.

Protoplasm may be conceived as a system in which in the interior fats, lipoids, proteins, etc., are dispersed by means of concentration films of soaps and other substances in water as an external phase, but that naked protoplasm, when coming in contact with water containing a variety of salts, tends to undergo a transformation with the formation of a film or membrane which consists essentially of a dispersion of water in oil, water in lipoid, or water in concentrated protein, a type of a jelly, or more probably a stage intermediate between those physical systems in which water is the dispersed and the continuous phase. The extreme outer layer consists, presumably, at least in part, of a mixture of soaps, and according to whether the soaps in question are more readily dispersed in water than in oil, lipoid, protein, etc., the film is more or less permeable to the passage of water and water soluble substances, and more or less readily dispersed or broken up and removed by the constituents of the external water phase.

Salts of calcium function invariably as protective agents for the films in question, preventing their dispersion or disintegration by substances present in the environing aqueous medium and interfering with a too great permeability of the protoplasm or protoplasmic film which, if carried beyond a certain point, would necessarily cause the destruction of the protoplasmic system.

The salts of calcium have been extensively employed by Wright and others to counteract sensitization and anaphylactic phenomena, for example, in counteracting oedema, urticaria, herpes, etc., induced as a result of sensitization to foreign proteins and against hay fever, asthma and other sensitization phenomena as in our experiments. In this and numerous other cases, calcium appears to function by protecting the surface film and preventing a too free passage of water and water soluble constitu-

ents. In the opinion of the writer, not only protoplasm but all colloidal aggregates present in the blood or body fluids are surrounded by stabilizing films, consisting at least in part of a mixture of soaps, which play the same role in maintaining the equilibrium of the protoplasm system and preventing the precipitation of proteins, lipoids, etc., by salts, as is played by the stabilizing soap films in emulsions in preventing the aggregation of individual globules of oil with one another.

Soaps exhibit an antitryptic reaction when present in the serum. Their removal from the serum by means of extraction with organic agents causes a reduction in the antitryptic index. It has been demonstrated by Bronfenbrenner and others that homologous serum extracted by means of organic agents is toxic for animals of the same species, and the suggestion has been put forward that the anaphylactic reaction is attributable to effects brought about by homologous proteins. In the opinion of the writer, the effects in question are attributable to the removal of stabilizing films of soaps or other lipoid disintegration products which are soluble in organic agents and the consequently more ready colloidal aggregation or precipitation of proteins and other colloids by electrolytes and other substances normally present in the system.

The writer has already demonstrated, in experiments which will be published shortly, that the antigen antibody combination in the presence of complement may function as a dispersing agent for fatty or soap films in colloidal systems of the type described above, and in others not yet described, from which it may be concluded that an anaphylactic shock represents a sudden and violent removal or partial destruction of certain protective colloidal films, thus causing a more free ingress of water and water soluble constituents to the interior protoplasmic constituents of the cell, with consequent destruction of the working mechanism of the cell. Effects of this type would obviously be produced, but with varying intensity, at different points in the body, and not only the cells but also proteins and other substances dispersed in the blood and other body fluids would be correspondingly affected.

The protective effect exerted by salts of calcium in physical and biological systems and also in animals and human beings exhibiting phenomena attributable to sensitization and anaphylaxis, is a strong argument in support of this point of view, and in a series of experiments published three years ago, the writer was able to demonstrate that the influence exerted by certain mixtures of powerfully absorbed divalent and trivalent cations with suitable anions exhibited exactly analogous curves in a comparison of effects produced on living mice, hemolysis of corpuscles by means of complement and amboceptor, the state of dispersion of colloidal systems in water, blood coagulation, and equilibrium of purely physical systems of the type described above. Since the hemolysis of corpuscles by means of complement and amboceptor serves in a sense as a model of the phenomena presumed to occur in anaphylaxis, and since this reaction is influenced by variations in the proportions of powerfully absorbed positive and negative ions in a manner very closely resembling the influence exerted upon purely physical colloidal systems and since the animals killed by intravenous injection of the salts in question exhibited symptoms resembling those of anaphylaxis it would appear probable that the phenomenon in question is attributable to variations in the state of colloidal aggregation of normal constituents of the body, under the influence of agents capable of producing sudden and violent dispersing effects. In advancing the theory that sensitization and anaphylactic phenomena are due to a sudden and violent increased dispersion of the external colloidal film of protoplasm and of the protective films of other colloidal aggregates in the body, and that the specific and nonspecific precedures employed to counteract these effects function by diminishing the intensity of the dispersion in question, and promoting aggregation of the films, we do not deny the possibility that side by side with the reaction in question and the exposure of naked protein to the influence of aggregating and subsequently of dispersing agents that a variety of disintegration products may

well make their appearance in the serum, but we are inclined to believe that the primary effect in anaphylaxis and the one that causes death is essentially a sudden disturbance in the colloidal equilibrium of the protoplasmic surface film, resulting in too great permeability of the protoplasm and a consequent irreversible disturbance of colloidal equilibrium of the protoplasmic system.

The CHAIRMAN. Inasmuch as my own communication is next on the program, I will ask Dr. Lung, of the United States Navy, to kindly take the chair.

The CHAIRMAN (Dr. Lung presiding). Ladies and gentlemen, Dr. Weil has already been presented to you and has addressed you. He needs no further introduction.

ANAPHYLATOXIN AND THE MECHANISM OF ANAPHYLAXIS.

By RICHARD WEIL,
Cornell Medical College, New York City.

I shall attempt to give simply an informal discussion of the subject of anaphylaxis as I see it. I have not prepared an elaborate paper, because I do not think the points which have been brought out lend themselves to a set discussion. They have been approached from a variety of standpoints, and I think that it is necessary to consider these various standpoints in a manner which I should not have been able to follow had I prepared my paper as I saw the subject before listening to these papers.

Dr. Bronfenbrenner alluded to the fact that I should probably have the difficult task of defending the cellular theory. I think that this statement is largely true. I shall indeed have that task, and with it goes the task of showing that the anaphylatoxins have nothing to do with anaphylaxis, because the two standpoints are entirely incompatible. Why it is that those two different problems have come to be associated in that way, I will show show you in a minute; but the fact is that they are intimately associated.

As regards the attitudes of the scientific world on the subject of anaphylaxis, I think you have probably gathered that it is not entirely harmonious, but it has taken a peculiar course in the United States. At the present time there is a tendency to accept the anaphylatoxin theory without question, owing largely to Jobling and others who have done so much work on anaphylaxis; and then, too, one must realize that the anaphylatoxin explanation of anaphylaxis is very enticing. It gives us a simple explanation for the phenomenon. A chemical toxin is said to be produced, and we are acquainted with the action of chemical toxins. We know that strychnin causes convulsions; well, then, in anaphylaxis they tell us a toxic substance is produced which acts in a similar way on the cells and gives rise to the symptoms. It is also enticing from the fact that it gives us a uniform explanation in that, according to Vaughan, the same toxic substances are always produced when antigen and antibody come together in the body, and therefore we always get the same exhibition of anaphylaxis.

This theory, however, is not universally held. For instance, Doerr takes exactly the opposite standpoint. Contrary to his previous view, inasmuch as he originally was a believer in Friedberger's theory that the reaction was humoral and that anaphylatoxin played a rôle, he has practically concluded in his last review to accept the cellular theory and at the same time he maintains that anaphylatoxin plays no rôle in anaphylaxis. Then there is Dale, in England, who holds the same theory, and Bayliss in his recent work on physiology, which I imagine is familiar to you all, uncompromisingly accepts this explanation. So, while this is a question of very

great importance for the general interpretation of the whole subject of immunity, and for the understanding of infectious diseases, it is one which at the present time has unfortunately not been entirely cleared up.

To give a brief view of the situation and to simplify it if possible, the following facts should be considered. The data of anaphylaxis and immunity, upon which we all work no matter what our interpretation is, are essentially two. We all agree that antigen and antibody are the factors involved. We all agree that antibody is present either in the cells of the body or in the blood of the body, or in both. We are all agreed that it is the interaction of these two factors which results in the phenomena of anaphylaxis and of immunity, strikingly different as are the manifestations involved—in one case an apparent protection against toxic substances and in the other case an apparent susceptibility to nontoxic substances.

Now, there are two questions that have been discussed to-day by Dr. Bronfenbrenner, Dr. Kolmer, Dr. Clowes, and myself, and they are the same questions which I tried to bring out in my initial discussion. The two questions are these: What is the site of the reaction in the body, and what is the immune mechanism? These are two separate questions, and yet, as you will see in a minute, the view which we take of one almost necessarily postulates the view which we shall take of the other.

As regards the site of the reaction, we are accustomed to distinguish between the humoral theory and the cellular theory, to which we might add an intermediate standpoint, which Dr. Kolmer advocates, viz, that the reaction may occur in either place.

If we look at the problem purely from an experimental standpoint, what facts are there in favor of the humoral theory, and what facts are there against it? As far as I know, there is only one experiment which supports the humoral theory, namely, the following: It has been maintained that if one introduces antigen and antibody into opposite jugulars of the same guinea pig or of the same rabbit, simultaneously, one gets anaphylactic shock. Now, that experiment is crucial. If the observation is correct, it is perfectly clear that the reaction in that instance is humoral simply because no time is given for the cells to anchor the antibodies; the reagents are simultaneously introduced, the reaction is instantaneous and must therefore take place in the blood stream.

If one comes to analyze the literature on the subject, however, one finds that none of the authors, with the exception of Gurd, has been able to state that this experiment has resulted in anaphylaxis with any frequency. In the great majority of instances the experiment has apparently no definite result. One can do it ad libitum, varying the relations as one pleases, yet in the great majority of instances one does not get the shock. This I showed some years ago. Gurd's experiments, however, seem to show that it occurs in a greater proportion of cases than we had thought; he himself maintains, indeed, that it can be produced with considerable regularity.

Accepting the fact that simultaneous injections do occasionally produce immediate death, how is this result to be interpreted? What is the result if one performs a control experiment—that is to say, if one uses an antigen and an antibody which are not at all related? Take the serum of a rabbit immunized to egg albumin as antibody, and horse serum as antigen, and inject them simultaneously into opposite veins. Even by this procedure one will kill the animals occasionally. There is here no relation of antigen and antibody, since you can not passively sensitize an animal by means of a previous injection of antiegg albumin serum and then intoxicate with horse serum. Therefore it seems clear that death in these cases is not an immunological phenomenon but is due simply to the simultaneous intravenous injection of any two foreign proteins. Unfortunately Gurd and none of the others who have worked at this phase of the problem had ever made this experiment, obvious as is the necessity of a "control" to their results. So that the one positive piece of evidence which has been advanced in favor of the humoral theory appears to be

utterly inadequate. Now, on the other hand, the positive evidence in favor of the cellular theory is very convincing, and all critics have accepted it, so that it requires only a superficial review.

If we take the uterus of a guinea pig which has been sensitized either actively or passively and suspend it in Locke's or Ringer's solution, it will trace a series of rythmic contractions. If we then add a minute amount of antigen, it at once executes a tremendous contraction. Here we have no participation by the circulation. The reaction occurs even if we have washed out the vessel before taking out the uterus. We have a response from the isolated cells. Friedberger made the objection that in spite of the washing out there was still enough antibody in the circumambient lymphatic fluid to produce the reaction, but I was able to show that this was not the case. Further studies have demonstrated the fact that during the latent period of passive sensitization the cells anchor the antibody; until this has been done, they fail to respond to the antigen. The time has come, therefore, to accept the cellular theory in toto. There is no reason to accept in the smallest part the humoral theory of anaphylaxis. The only argument that keeps us still tied to the latter theory is the fact that the men who believe in anaphylatoxin somehow feel themselves bound to support the humoral theory in order to sustain the test-tube experiment. Yet this is an unwarranted assumption. The cell might conceivably functionate as a test tube in which antigen reacting with antibody might produce the same sort of changes, whether they be chemical or physical, as are ordinarily ascribed to the production of the so-called anaphylatoxin in the test tube. It is therefore an illogical non sequitur which Friedberger originally committed, and which seems to have gone down through the years, that influences men who accept the anaphylatoxin theory to believe that they are thereby committed to the humoral theory.

This brings us to the second question, the question of the immune mechanism. Now the immune mechanism has been described briefly in the talk which I gave at the outset. There are practically two theories, the physical theory and the chemical theory. Both of these theories accept the fact that anaphylaxis is the result of the reaction between antigen and antibody. They differ, however, in one respect. The chemical theory maintains that there is an intermediate process and that when these two substances interact a chemical substance is formed which actually produces the toxic symptoms. The physical theory ignores any such intermediate step and maintains that simply in virtue of the attack of antigen upon the antibody of the cell that cell is stimulated just as it would be by an electric shock or by any other sudden physical change. These theories are not of merely scholastic interest. The entire philosophy of immunity is involved in the choice between them. The school that accepts the anaphylotoxin theory believes that the mechanism of anaphylaxis and of immunity is essentially the same and that anaphylaxis and immunity are practically identical phenomena, which differ only in degree. Those who originally advanced the chemical theory explained the difference in the following manner: They said that antibody in the presence of antigen acts on the latter as a proteolytic ferment and breaks it down. If there is relatively little antibody, as after a single injection, the breaking down of the antigen is incomplete and slow and results in the production of the higher proteoses which are toxic and which kill the animal; this is anaphylaxis. If, however, the blood is rich in antibodies, as after repeated injections, the breaking down of the foreign proteins is rapid and goes to the limit with the production of amino acids, which are not toxic; and this is immunity.

Now Dr. Bronfenbrenner has altered the terms of this explanation somewhat. He says that the breaking down of the animal's own protein results in anaphylaxis instead of the breaking down of the antigen; but, as you see, the same chemical process is involved in this theory.

The physical theory is as different from this as it can possibly be. According to the physical theory anaphylaxis results when the antigen attacks cells containing antibody. On the other hand, when there is sufficient antibody in the serum to ward off the antigen from this attack on the cells immunity results. Thus the process of anaphylaxis and of immunity are fundamentally opposed; there is the union of antibody and antigen in the serum, which protects the cells against the antigen; when the two unite in the cells, however, we get the explosive and the unfortunate symptoms of anaphylaxis. So you see our whole conception of immunity is materially affected by our interpretation of the mechanism of anaphylaxis.

To come to the evidence in favor of anaphylatoxin and the evidence against the action of anaphylatoxin in the animal. We all know, and we are all willing to admit, that we can produce substances which are toxic by the incubation of sera under various conditions outside the body. These substances are often classed together under the name "anaphylatoxin." Historically speaking, this substance should not be called anaphylatoxin. The phenomenon was originally observed by Richet, who called the substance apotoxin. As you know, anaphylatoxin has been produced by the incubation of serum with a great variety of substances.

Now the question is, does this effect of incubating serum with various substances outside the body justify us in believing that the same process occurs in the body. As a matter of fact it does not. Agar incubated with serum produces a toxin, but agar injected into the circulation is harmless. The only way to prove that the processes are similar is to take the blood of an animal in anaphylactic shock and determine whether it contains such toxic substances. Such experiments have been reported by Thiele and Embleton with positive findings. Personally I have been unable to reproduce their results, and Doerr in his latest review has shown that their experiments are open to serious criticism. Thus there is no experimental evidence that any such substance as anaphylatoxin is produced in the body. There is in fact every reason to believe the reverse. As a matter of fact, the anaphylatic phenomenon is strikingly unlike the effect of a toxin. An animal goes into shock, into convulsions; but if it recovers within 10 minutes it may be eating its food just as if nothing had happened. It acts as if a violent shock or stimulus had been received, not as if poison were circulating in its blood. It is the same with the experiment of the suspended uterus. You can get it to contract violently by adding antigen and get it to relax by simply changing the fluid; and at the end of such a series of anaphylactic responses the uterus seems as normal as ever.

There are, however, additional insuperable objections to the analogy between anaphylaxis in vivo and the production of anaphylatoxin in vitro. In the first place, there is the matter of specificity. We know that anaphylaxis is a specific phenomenon. It is just as specific, or almost as much so, as the precipitation or the agglutination reactions; the anaphylatoxic substances on the contrary, can be produced under the most varied circumstances. Incubation of serum with the most diverse substances is equally effective in this regard. Then, there are various other conditions, which I have already briefly sketched, when anaphylatoxin is produced by incubation. The process requires relatively considerable periods of time, and the proportions of antigen and antiboby can be varied only within narrow limits. Now, the striking thing about anaphylaxis is that the reaction does not require time. In the living animal the minute the injection is made into the jugular the animal goes into convulsions. As Dale has shown, in the uterus the reaction also is immediate. Again, as regards proportions of the two factors, conditions in the animal are quite different. If an animal is passively sensitized against horse serum by an injection, let us say, 0.1 cc. of rabbit, immune serum can be killed with 1 cc. or 0.01 cc. or 0.001 cc. of horse serum. In these particulars, therefore, the production of anaphylatoxin in the test tube has no resemblance to the vital reaction.

Either upon the cellular or the humoral theory, then, the anaphylatoxin theory is entirely inadequate. It fails to satisfy any of the demands of the problem. There is, of course, no question that anaphylatoxin is produced in vitro; but we should not blind ourselves to the fact that this has nothing to do with the interpretation of anaphylaxis. Such a conclusion does not necessarily detract from the interest or the importance of the work that has been done on anaphylatoxin, but it does suggest the idea that some other term should be used in describing these toxic products. Perhaps the term originally suggested by Richet, "apotoxin," is as good as could be devised.

As bearing upon this problem of the relationship of anaphylatoxin, I hope that you will permit me to describe certain new experiments which are designed to answer questions in the mechanism of anaphylactic shock. In the first place, what is the antibody concerned in anaphylaxis? Originally Friedberger and Doerr maintained that it was precipitin, and they showed that, as a rule, the curve of precipitating antibodies in the serum runs a course parallel with the sensitizing value of the same. It has, however, been shown that this parallelism does not hold in active anaphylaxis; that guinea pigs might be highly anaphylactic and still have no precipitin in their serum. The following experiment seems to throw light on this question: One takes the serum of a rabbit immunized to horse serum and horse serum, mixes them, incubates them for a short time, and gets a precipitate; centrifuges the precipitate, pours off the fluid, and retains a precipitate entirely free from the supernatant fluid. If this precipitate is taken up in salt solution and injected intraperitoneally into a guinea pig, one can sensitize this guinea pig passively with that precipitate. If one waits three days and then injects the antigen, the animals are found to be sensitized exactly as if they had been given rabbit vs. horse serum. This shows that the precipitin is the same as the sensitizing antibody. I will not go into the controls which were used.

The next question which arose was, Is the precipitating function necessary for sensitization? Now, if this serum is heated to 72°, it loses its precipitating function, but it still unites actively with the antigen. That has been proved by other experiments. If one takes a serum heated in this way to 72°, although it has lost its precipitating function entirely in the test tube, it retains, although slightly diminished, its sensitizing value for the guinea pig. Now, I think that proves definitely that the precipitating function is not necessary to the anaphylactic phenomenon.

This leaves us simply the combining group, the haptophore group, as the factor concerned in sensitization. This conclusion harmonizes with the so-called physical theory of anaphylaxis—viz, that it occurs when the cell possessed of an antibody anchors circulating antigen. The very fact that they unite stimulates the cell to the response.

The question remains, How does complement enter into the reaction? You know that when the precipitating antibody unites with antigen it also anchors complement; we find that when serum is heated to 72° it loses the power of binding complement; when it is heated to 56°, which is the control experiment, it still binds; and yet, when we compare the sensitizing value of serum heated to 56° with that heated to 72°, it differs very slightly. And I think that this proves that complement plays absolutely no rôle in the reaction, and that here we have definite proof of the fact that in the body the binding of complement plays no rôle in the anaphylactic reaction. The anaphylotoxin theory is also implicated in this conclusion. You can not get anaphylatoxin in the test tube by incubating antigen and antibody unless complement is present. So, here is another argument, which I believe is final, as to the inadequacy of the anaphylatoxin theory.

The other questions in the interpretation of anaphylaxis and immunity are subsidiary questions. The points that I wish to impress upon you are: (1) That the theoretical evidence and the experimental evidence are absolutely against the humoral theory; (2) that it is no longer possible to straddle the problem by maintaining that anaphylaxis is preeminently cellular, but occasionally humoral; and that (3) anaphylatoxin plays no rôle whatever in anaphylaxis.

The CHAIRMAN (Dr. Weil presiding). The discussion is now open on these papers.

Dr. BRONFENBRENNER. Gentlemen, the fact alone that Dr. Weil preferred to spend most of his time to criticize the humoral theory of anaphylaxis instead of presenting his own paper shows how important he considers the difference between this and the cellular conception of anaphylaxis. My paper was not intended to emphasize the humoral theory at the expense of cellular, though the material presented by me does, in a way, illustrate the statements made by the representatives of the humoral theory of anaphylaxis.

Personally, I have not worked in anaphylaxis much and my interest in the subject arose from the work on abderhalden reaction. Though as a pupil of Prof. Besredka in 1909 I have been engaged in some of the experiments in anaphylaxis under his direction, my views as to the mechanism of anaphylaxis are not entirely those represented by the humoral theory. I think, however, we should not hurry to discard any one of these theories, even if one of them happens to be the older one. Not all that is old is bad. Insomuch as the humoral theory is able to explain all the phenomena which it is supposed to explain (many workers think it can), there is no need of discarding it in toto and replacing it with the other, even if certain experiments, performed by its adepts, undoubtedly demonstrate the possibility of cellular response being an integral part of anaphylactic shock.

As Dr. Clowes has remarked a few minutes ago, the phenomena in anaphylaxis are very general; if they affect one structure of the body, they must similarly affect other structures of the body, as there is no essential difference between serum and the tissues which the serum envelopes.

Although there are many phenomena which can not be adequately explained by the cellular theory of anaphylaxis, I do not intend to go into their discussion, for it would take again as much time as we have consumed. The experiments quoted by Dr. Weil undoubtedly suggest that it is possible to demonstrate cellular reaction in anaphylaxis. Without denying that, my own experiments suggest that anaphylaxis may be produced as a result of the combination between the antigen and antibody of the blood. Of course, as Dr. Clowes has stated, the cells of the body take a very essential

part in the reaction. In fact, as I understand it, the very moment antigen and antibody unite there occurs a change in molecular dispersion (which can be demonstrated in the experiments in vitro.) In the body this change in the physical state of serum (through its combination with antigen) affects the physiologic functions (permeability?) of the cells so that a number of cells may even die as a result of this change. Whether in this process there is formed an intermediate toxic product (anaphylatoxin) which is a distinct chemical substance, I do not know. I think anaphylatoxin is not similar to the toxic substances of Dr. Vaughan. I am more inclined to view anaphylatoxin merely as a stage in the physical change the serum is undergoing, the change which is characterized by its deleterious effects on the life of the cells (possibly by affecting the permeability).

Referring to Dr. Kolmer's discussion, I would like to ask whether I understood Dr. Kolmer correctly? Dr. Kolmer thinks, I believe, that there is no doubt of the specificity of the ferment in pregnancy. If so, I disagree with him. I have shown in my published work that the ferment concerned in the abderhalden reaction is not specific. The apparent specificity of the reaction is due to the mechanism of the activation of the normal blood ferment by the combination of the antigen (placenta tissue) and antibody present in the blood of pregnant women.

Dr. KOLMER. My remarks will be very brief. Like Dr. Bronfenbrenner, most of the work that I have been doing has concerned the mechanism of the abderhalden reaction and I based my belief—tentative belief—on the presence of a specific ferment from the fact that digestion as we are able to measure it by all methods, except the more recent one of Von S would show that digestion of placenta by the serum of a pregnant woman was more intense than of non-pregnant, and I advanced that as an argument against the purely chemical theory, as it were, that it is the mere absorption of antiferment that results in digestion.

As to Dr. Bronfenbrenner's question relative to my belief in the specificity of the ferment, I may say that I put this reprint to which Dr. Bronfenbrenner refers in my pocket this morning with the idea of asking him, if I had a few minutes, his own idea about it, because I find in the same reprint the statement that they are non-specific and then on the next page that they are specific.

As I wrote my paper only in the last day or two, it was my object rather to review the present opinions particularly in reference to abderhalden reaction. My own belief is that there is in pregnancy a specific ferment.

Dr. BRONFENBRENNER. According to my findings the specificity lies not in the nature of the ferment, but in the nature of its activation. I wish to make it very plain. The ferment is not specific.

The same ferment is present in pregnant as in nonpregnant individuals, but it may be made active in the serum of pregnant individuals by the specific process of the union between the specific antibody such serum contains (in addition to the nonspecific ferment) and corresponding antigen. The molecule of the protein of the serum having a certain structure, if the specific combination of antigen and antibody will change the degree of dispersion of the particles in it, would be broken up—digested. The end result appears to be specific, but the mechanism is not that of the action of a specific ferment.

The CHAIRMAN. We come now to the paper of Dr. A. P. Hitchens and Dr. C. P. Browne, "Hay fever and certain other local anaphylactic phenomena referable to the respiratory mucous membranes."

Dr. HITCHENS. On account of the lateness of the hour and the length of our paper, I should like to suggest, if Dr. Brown will agree, that our paper be read only by title. It will probably be published, and I think every one may get as much from the abstracts possibly, as from the whole paper. Those who are especially interested may read the published paper.

HAY FEVER AND CERTAIN OTHER LOCAL ANAPHYLACTIC PHENOMENA REFERABLE TO THE RESPIRATORY MUCOUS MEMBRANES.

By A. PARKER HITCHENS AND CLAUDE P. BROWN, *Glenolden, Pa.*

In reviewing the history of hay fever we find that the literature naturally falls into five fairly distinct periods:

First period.—In the earlier bibliography, long before the first accurate description of the disease by Bostock (1) [1] there are numerous references to periodical attacks of rhinitis and asthma as well as to various idiosyncrasies associated with flowering plants. Among the earliest of these is Botallus (2)—"for there are many who are attacked with sneezing, by the slightest thing whatsoever, others by merely smelling a rose." [2] Others mentioned by Sticker (3) are Binninger (4), Ledelius (5), Hünerwolf (6), and Constant de Rebecque (7). Bostock stated that the earliest reference to which his attention had been called was that of Heberden (8). The quotation referred to is probably "Five patients were attacked violently by this disease for a month every summer; one was afflicted annually for the entire summer; another was never free from it except in the summer." [3] These references are sufficient evidence that hay fever existed for centuries before its recognition as a specific disease and all attempts to estimate its antiquity are entirely futile.

[1] Figures in parentheses, used as references, refer to publications bearing identical numbers, under the head of "Bibliography," at the end of this paper.

[2] "Nam plerique sunt qui quacunque re levissima sternutationis multis agitabuntur, alii ex solo rosae odoratu."

[3] "Quinque aegris contigit graviter laborare hoc morbo per mensem omni aestate; alium totam aestatem afflixit quotannis; alius nunquam nisi aestate ab eo liber fuit." In a translation of Heberden's work published the next year (9) is the following: "I have known it return in four or five persons annually in the months of April, May, June, or July, and last a month with great violence. In one a catarrh constantly visited him every summer: and in another this was the only part of the year in which it ceased to be troublesome."

Second period.—In 1819, Bostock (1) described a "Case of a periodical affection of the eyes and chest" so accurately that later writers, even in their most elaborate analyses of symptoms, have been able to add nothing of clinical importance. The attention of other physicians thus being called to this affection, reports in a short time began to appear in the medical publications of England, France, and Germany. Nine years later Bostock (10) himself added distinct accounts of 18 cases, with 10 others "less correctly ascertained." Elliottson (13) contributed a number of cases and noted many interesting data with regard to the association of symptoms with the apparent exciting causes. From the contributions of Gordon (11) and Macculloch (12), we learn that the term "hay fever" was probably used some time before its recognition as a disease by Bostock.

Our information concerning the incidence of hay fever, its relation to age, sex, and condition of life, and its geographical distribution may be attributed in some degree to Elliottson (13) but still more to Phoebus (14).

With regard to the etiology, various theories were held and practically every external agency was claimed at first as an exciting cause. Bostock believed his own symptoms to be due to the heat of summer, while other writers held the odor of flowering plants chiefly responsible. The proposal of a bacterial origin by Helmholz (15) never gained much headway. Pirrie (16) suggested that the disease was of nervous origin, at the same time admitting emanations from plants and various external agencies as exciting causes.

In 1859 Prof. Phoebus (14) of the University of Giessen, sent out about 400 circulars to physicians, medical societies, etc., requesting information concerning hay fever. His analysis of the replies received remains one of the best statistical studies of the disease, but no fundamental facts with regard to etiology were ascertained. One of the most interesting communications quoted by Phoebus (14, pp. 136, 137) was that of Kirkman, who disagreed with the opinion that emanations from *Anthoxanthum odoratum* were a cause (probably the cause, according to Gordon (11), because "I am always attacked at least three weeks before the *Anthoxanthum* is in blossom." Later, in his hothouse, he noticed, a day or two before Christmas, a single *Anthoxanthum odoratum* in blossom and well loaded with pollen. He rubbed the flower in his hand and sniffed it, whereupon all the symptoms of hay fever appeared immediately, continued for an hour, and then left him.

In 1872 and 1876, respectively, Morrell Wyman (17) and Beard (18) published statistical investigations similar to those made by Phoebus. Although Blackley's work had appeared three years earlier, Beard was confident that his theory of a nervous diathesis was conclusive; he said that pollen was merely one of the "debilitating influences, exciting causes purely, and of themselves are powerless to induce, or at least to sustain an attack."

Third period.—The chaotic state of these earlier opinions could be cleared up only by actual experiment. However little serious attention it attracted at the time, this necessary elucidation was furnished by Charles H. Blackley (19), a physician of Manchester, England. In 1873, he published the results of one of the most complete researches in the history of experimental medicine. Blackley, himself a sufferer from hay fever, was at first inclined to agree with Bostock that summer heat was the cause of the disease, but he was led to question the correctness of this view by circumstances connected with a journey to the sea coast. In the locality of his home at Manchester the hay had already been gathered in and his attacks of hay fever had ceased; on approaching the sea coast, however, the symptoms reappeared, and later investigation revealed a field of uncut hay, much of which was in flower. His attention was directed to the same subject by an incident two years later. Upon examining a bunch of grass brought indoors by one of his children the cloud of pollen scattering near his face brought on violent sneezing in two or three minutes. Blackley dates his experimental work from this time (1859).

After carefully reviewing all the current opinions concerning the etiology of hay fever Blackley asked himself the following questions:

First. Can pollen produce the symptoms of hay fever?

Second. Does this property belong to all the pollens or is it confined to the pollen of some one or more orders of plants? And if so, to what natural orders does it belong?

Third. To the pollen of which natural order, or of which species of this order, are the actual attacks of hay fever, as they occur in early summer, due?

Fourth. Is this condition or property found in the dried as well as in the fresh pollen?

Fifth. To what special substance in pollen is this supposed action due?

In order to answer these questions, Blackley experimented upon the pollen in five different ways: "First, by applying it to the mucous membrane of the nares; second, by inhaling it, and thus bringing it into contact with the mucous membrane of the larynx, trachea, and bronchial tubes; third, by applying a decoction of the pollen to the conjunctiva; fourth, by applying the fresh pollen to the tongue, lips, and fauces; fifth, by inoculating the upper and lower limbs with the fresh moistened pollen."

Blackley (19, p. 75) tested on himself the pollens of the grasses and of plants belonging to 35 other natural orders, all of which produced symptoms. He studied microscopically the various pollen grains; furthermore, he counted the grains deposited within a given time upon slides coated with glycerine and carbolic acid. These studies were made at different seasons, indoors and out, in country and in city, at about the level of a man's head and at higher altitudes by means of kites. Blackley demonstrated that symptoms did not appear until the pollen grains had reached a certain number, and that the severity of the symptoms varied in direct ratio with the amount of pollen in the air. He also showed that pollen may travel enormous distances, thus accounting for the fact that the seashore, or even the ocean, does not always afford relief to susceptible persons.

In all this work Blackley himself was the subject of the experiment. At that time he tried in vain to find other hay-fever sufferers who would submit to the tests; however, the opportunity came to him later (20) to corroborate his findings on other patients.

In spite of the evidence presented by Blackley, the attention of his contemporaries was so concentrated upon the work of Pasteur and Koch that no suggestion regarding etiology was welcome unless founded upon bacterial infection. The findings of Helmholz that a vibrio was the cause of hay fever were confirmed by Binz (23) and Patton (24). Heymann and Matzuschita (22), however, attempted to straddle the question by suggesting pollen as the carrier of bacteria, especially of streptococci.

Furthermore, the fact that Blackley's work contained no facts of direct therapeutic value naturally detracted from its significance for clinicians. Thus, it was not until the successful application of Noon's method of vaccination that the etiologic rôle of pollen attracted general interest and found final acceptance to the exclusion of all other theories.

Fourth period.—In 1903 Dunbar (21) published his work, built upon the foundation laid by Blackley. With technique similar to that used by his predecessor, Dunbar experimented upon himself and other susceptible persons, with the result that pollen was established as the cause of hay fever. Thus the findings of Blackley were confirmed. Dunbar believed at first, however, that only certain pollens were in question. This point is still unsettled and needs further investigation.

Dunbar was more fortunate than Blackley in having at his disposal the results of all the later achievements in both organic chemistry and immunology. The latter was an unknown science in Blackley's day. Dunbar's work on the chemistry of pollen thus constitutes a real advance in our knowledge of hay fever. In the field of immunology he was able, by serological tests, to strengthen the evidence in favor of the etiologic rôle of the pollen proteins. He was the first to establish the possibility

of active immunity and to elaborate a specific therapy, but he fell into error by applying to hay fever the discoveries of Behring, Kitasato, and others concerning bacterial toxins and antitoxins. Dunbar maintained that hay fever was caused by a true toxin existent in the pollen, and that the serum of animals (rabbits and horses) injected with pollen and pollen derivatives possessed true antitoxic power. At present we regard hay fever as an anaphylactic phenomenon, and consider that the serum elaborated and patented by Dunbar [1] belongs with the antibacterial serums; in other words, that it depends for its activity upon amboceptor and not upon antitoxin.

Fifth period.—In 1911 Noon (25) reported the results of his work in the laboratory of Sir Almroth Wright on the treatment of hay fever with subcutaneous injections of pollen extracts in minute doses. Curtis (26) and Dunbar had previously used plant extracts and pollen extracts, but neither of them had achieved results sufficiently promising or reliable to encourage a continuation of their work. Noon injected extracts of timothy pollen, controlling the doses by ophthalmo reactions; this work interrupted by his untimely death, was continued by Freeman (27).

Preparation of pollen extracts.—Dunbar (28) and his associates, Prausnitz (29), Kammann (30), Weichardt (31), and Liefmann (32), demonstrated that the protein which constitutes about 40 per cent of the organic substances in pollen, is the active agent in causing hay fever. Accordingly, all methods in the preparation of material for vaccination must include extraction of this essential protein.

One of the methods used by Dunbar for the preparation of his "pollen toxin" is to extract the finely pulverized pollen with 5 per cent sodium chloride solution containing 0.5 per cent phenol, incubating the mixture at 37° C. The undissolved portion removed by centrifugation consists of empty pollen membranes and inactive starch rods. The supernatant opalescent solution contains the dissolved proteins; this is intensely active, even in high dilution, when applied to the skin or conjunctiva of susceptible persons. For use, the extract is diluted with physiological saline solution. He suggests further purification by precipitation with eight (8) volumes of absolute alcohol or by dialysis. Only the albumens, which constitute about 16 per cent ot the total proteins, are toxic, the globulin fraction being entirely inactive.

Subsequent investigators have made their extractions with distilled water and with saline solutions of various strengths. The pollen is sometimes ground with sand; Goodale (43) considers grinding unnecessary.

There are other modifications in technique which are scarcely worth mentioning. In many instances the possibility that the extract is not sterile can not be eliminated. Standardization is generally considered accomplished by noting the relation between the quantity of fluid and the amount of pollen extracted. This procedure is obviously subject to great variation. Cooke's (41) method of standardization seems to be the most accurate so far, and it is the one we have adopted.

Recent literature.—Among the recent reports of Clowes (35), Lovell (36), Lowdermilk (37), Ulrich (38), Koessler (39), Manning (40), Cooke (41), Wood (42), and Goodale (43), the observations of Ulrich regarding intervals between doses are of special interest. He noted that some patients were relieved for much longer periods than others, and because of this variability in individuals, he suggested that the intervals be governed in each case by the date of return of the symptoms.

The excellent technic of Cooke (41) with regard to standardization has already been mentioned. His theories regarding the mechanism of hay fever and its treatment are in accord with the latest views of anaphylaxis:

1. *With regard to antibody formation.*—It must be borne in mind that any form of foreign protein parenterally introduced within the living body gives rise to the formation of a specific immune or antibody which exists either attached to certain cells or free. When union takes place between protein and free antibody, there is no clinical evidence of a reaction, but when a union takes place between protein and

[1] D. R. P. No. 152163.

fixed antibody, a reaction takes place, and the nature of this reaction is determined by the type of cell to which the antibody was attached.

2. *Relation between immunity and anaphylaxis.*—They are qualitively identical but quantitatively different. In other words, when there is a large excess of antibody circulating free we have an immune state; and when there is little antibody, and that for the most part attached, we have the sensitized state.

3. *Duration of immunity.*—Immunity in the sense that free excess antibody once present is always present does not exist. With cessation of protein injection, the body returns to the anaphylactic state, in which it may remain, or to the state of accelerated capacity to form antibody.

The attempts of Goodale (43) to classify the susceptibility of patients according to natural orders, and thus to study this part of the problem systematically, opens up many interesting possibilities not only in hay fever treatment but also in botanical classification.

Work of the writers.—For obtaining the pollen the flowers are gathered just when pollination has started. The flowers are dried and the pollen collected by means of fine sieves. The pollen itself is thoroughly dried immediately and preserved in the dry state until it is to be extracted.

1. The pollen is mixed with sufficient physiological saline solution (0.85 per cent) to make a fairly thick paste.

2. The paste is transferred to a porcelain ball mill and ground for 24 hours, or until microscopic examination shows that the pollen grains are broken,

3. Physiological saline solution is added and the resultant mixture is centrifuged to remove insoluble débris.

4. The extracted protein is purified by precipitation with acetone.

5. The precipitate is dried and thus preserved until needed.

6. For use, the precipitate is dissolved in physiological saline solution. The amount of protein-nitrogen in this solution is determined by the Kjeldahl method.

7. The solution is then diluted so that each cubic centimeter will contain certain fractions of a milligram of protein-nitrogen.

8. The lowest dilution, 1 c. c. of which may be used as the initial dose in treatment, contains 0.0025 mg.

9. The final solutions are preserved from contamination by the addition of 0.25 per cent three cresols and sterilized by filtration. Sterility is determined by careful aerobic and anaerobic cultural tests.

The treatment may be continued with increasing multiples of this amount according to the needs and the sensitiveness of the patient. The injections are first given at about 5-day intervals, but as soon as the period of relief has been found these intervals are shortened or lengthened, that is, if treatment is necessary during the season.

We consider this better technique than to depend upon ophthalmo reactions which may be dangerous or upon skin tests which merely complicate the procedure for the clinician. In other words, ophthalmo reactions and skin tests bear the same relation to pollen vaccine dosage that the opsonic index bears to bacterial vaccine dosage. By the ophthalmic test Noon and Freeman were able to place pollen vaccination upon a scientific basis similar to that achieved by Wright by means of the opsonic-index technique. At present by starting with a dose (of either vaccine) demonstrated to be sufficiently small to do no harm satisfactory results are obtained without the same control of dosage that was necessary at the beginning.

Our spring extracts contain a mixture of the pollens of redtop, timothy, rye, sweet vernal grass, and orchard grass; the autumn type consists only of ragweed.

These vaccines have been used by ourselves and by other physicians kindly cooperating with us in the treatment of 61 patients.

Of these 61 cases 17 had asthma as a complicating symptom, of which 3 gave no report, 1 was not relieved, 2 were considerably relieved, and 11 were entirely relieved. Of the 44 remaining cases, 3 gave no report, 2 were not relieved, 4 were slightly relieved, 18 were considerably relieved, and 17 were entirely relieved.

One patient has apparently been cured. He was treated during two years in both spring and autumn. Another patient, who was only partially relieved, was found to be susceptible to wheat, but he was compelled to leave the vicinity before a special extract could be prepared for him.

One patient not completely relieved by the spring vaccine was found susceptible to daisy pollen. A special "daisy" vaccine was prepared, and the administration of a single dose brought complete relief.

Our results, on the whole, do not differ greatly from those obtained by others since Noon's first report. In none of these cases have we considered the possibility of a superadded or even possibly of a primary bacterial infection. This point, however, should not be overlooked.

Alexander (34) reports two patients suffering from chronic nasal catarrh, which condition was aggravated by pollen during the hay-fever season. Treatment with Noon's pollen vaccine had no effect. But after bacteriological examination and the administration of micrococcus catarrhalis vaccine the cases were cured.

We have treated one asthmatic patient with bacterial vaccines who throughout one winter did not have a single attack, although each winter previously she had experienced many.

Other anaphylactic phenomena.—The validity of the so-called idiosyncracies to the emanations from animals can not be questioned. Inquiry into the cases of sudden death following the injection of horse serum has shown that many of these persons had previously suffered asthmatic attacks whenever coming in contact with horses.

The manifestations of anaphylaxis after eating certain foods are now well recognized. All these facts lead to the deduction that any protein in the atmosphere may find hypersusceptible individuals who react with sneezing and all the symptoms of hay fever or asthma, or possibly with other more obscure symptoms. A case in point is the effect of bad ventilation (or the lack of ventilation) on certain persons while the other occupants of the room remain unaffected. Rosenau and Amoss (33) have attempted to demonstrate the presence of proteins in the exhaled breath, and although this work as yet lacks confirmation we believe it is a line of research worthy of closer attention.

Discussion.—We feel that possibly an explanation should be offered for consuming so much time with the history of hay fever. However, we believe this review to be fully justified if, by clearly outlining the work already successfully completed, we may thereby indicate the departments of this subject actually in need of closer investigation.

Hay fever at present is a problem of immunology and of chemistry, and the extension of our knowledge is limited to these two fields unless some unsuspected development may lead to a departure from the present trend of research—a departure such as followed the investigation of anaphylaxis by Rosenau and Anderson.

The demonstration made by Noon that injection of a pollen extract, under the rules laid down by Wright, has immunizing and therapeutic value in hay fever suggests two important questions:

1. What essential constituent of the pollen should be contained in the extract? This is practically question No. 5 asked by Blackley, and the work of Dunbar and his associates has gone far toward giving us an answer. However, the lack of a standard method for preparing an extract of maximum diagnostic, immunizing and therapeutic value, clearly indicates the intensive investigation needed in this direction. Whether or not the same constituent would possess all these properties would be one point demanding further study.

Although the method adopted by us is not the best possible, it is in certain respects superior to some of those described in recent reports.

a. Keeping qualities.—Koessler (39) among others found his extracts to be worthless after 3 weeks. An extract prepared by the technique given above yielded positive

therapeutic results after 2 years; chemical tests according to the Kjeldahl, biuret, and Sörenson methods showed neither any change in protein-nitrogen content nor decomposition with formation of peptones or amino acids.

b. Uniformity.—The Cooke method of standardization certainly appears more rational than that used by Dunbar and others who estimate the strength of the extract by the amount of pollen submitted to extraction. Lack of uniformity in the strength of his vaccines may account for the fear of anaphylactic shock expressed by Lowdermilk (37). None of our patients had more than a slight local reaction which caused no inconvenience.

2. To what pollen is the individual patient susceptible? This is Blackley's Question No. 2. While certain patients are susceptible to the pollen of only one or a very few plants (or at least to a single natural order), others, like Blackley, are susceptible to nearly all plants; there are, of course, all grades between. Goodale has attacked this problem from a practical standpoint by classifying the various pollens with a view to minimizing the number requisite in treatment. Freeman reduced his vaccine to an extract of timothy pollen alone. It would greatly simplify matters for the clinician if in the fall the pollen of a single member of the Compositae could be applied. A sufficient number of cases has been reported, however, to show that some patients would not be relieved, even assuming that timothy pollen extract and rag-weed pollen extract are adequate for the Gramineae and the Compositae, respectively. Persons susceptible to rose pollen or to the pollen of certain trees are cases in point.

Although these two questions are the most important at the present time, a third problem is ever present with the practicing physician.

3. In the present state of our knowledge of hay fever, how can this knowledge be best applied to the advantage of our patients? The answer to this question may be considered in two sections: (*a*) Measures to be taken two or three months before the hay-fever season, and (*b*) measures to be taken immediately before or during the hay-fever season.

a. Measures to be taken two or three months before the hay-fever season. When the patient can be studied beforehand, a survey of his habitual surroundings should be made. After noting all the flowering plants which might reasonably come into question, skin tests should be made with pollens of each of these plants in order to determine which of them are responsible. In this connection it must be remembered that pollens may travel great distances (Blackley). Accordingly, a field of grain even several miles away must be taken into consideration.

It seems scarcely necessary to mention the eliminations that could be made according to the seasonal incidence of the attack. The *Gramineae* in the spring, the *Compositae* in the fall would receive first consideration.

b. Measures to be taken immediately before or during the attack. If the attack has already started, treatment should be begun at once with a vaccine representing the pollens most likely to be responsible for the attack. If the treatment does not give entire relief, an exact diagnosis may be made quite independently of the treatment.

While the ordinary seasonal attacks can be controlled fairly easily, those patients who suffer from earliest spring until latest autumn may present greater difficulties. As stated above, we have treated one patient of this type during two springs and autumns with apparent cure as the result.

As regards dosage we believe that the placing of extracts upon the conjunctiva should be unqualifiedly condemned. Skin reactions may not be quite so exact, but they are adequate for all practical purposes, if indeed any such control is needed, except in diagnosis.

In conclusion, we wish again to suggest that those persons now investigating hay fever first familiarize themselves with the magnificent research of Blackley, as well as with the chemical studies of Dunbar and his associates. Among the innumerable

publications there are after all only a few that are of vital importance—the works of Bostock, Blackley, Dunbar, and Noon. Many other compilations are extremely interesting, notably the reports of Phoebus and Sticker, but they serve merely to confirm or elaborate previous knowledge of the disease.

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Dr. Lung presiding.

Dr. WEIL. Mr. Chairman, I do not believe you can combine incompatibles. Either one of the two things is correct, and I do not believe that it amounts to the same thing to say that it occurs inside the cells or that it occurs outside the cell. If it occurs within the cell, as Dale has pointed out repeatedly, and as Bayliss has confirmed —and as I believe, as far as I can follow the discussion, Dr. Clowes also believes—if it occurs in the cell, it is a physical phenomenon. If it occurs in the serum and anaphylatoxin is part of the mechanism, it is a chemical phenomenon and can be produced by incubation. Now, it does not do to try to combine those ideas. One of them is correct and the other one is wrong, and whichever point of view is eventually accepted, the other one will have to be given up. I am not here to try to prove to anybody that one is absolutely right and the other absolutely wrong. Of course, my own conviction has been stated. It is not, Dr. Bronfenbrenner, that the humeral theory is conservative. The first theory was the cellular theory, advanced by Otto, accepted by Friedberger, and was the older theory. That was given up later by Friedberger, when he fell in love with anaphylatoxin, and subsequently the cellular theory has been advanced by Dale and by Doerr, who has come to adopt it.

Dr. CLOWES. I just want to make it clear that I am in favor of the view that it is physical.

The CHAIRMAN. If there is no objection we will hear from Dr. Clowes.

Dr. Weil took the chair.

Dr. CLOWES. We have studied in the last few years a very large number of cases of hay fever, some hundred or so. As you know, Dunbar, Wright, and others worked on the subject. I think that we were the first to demonstrate that it is possible to immunize against the autumnal form of hay fever by injecting extracts of the pollens of ragweed and goldenrod. We test cases by the ophthalmic and the cutaneous reactions. To those who would like to see

a demonstration, I may say that I happen to be susceptible to ragweed and can thus far show the tests on myself. The treatment is successful in 30 to 40 per cent of individuals when they are immunized against the particular form of pollen to which they are sensitive.

The group reactions of pollen are very interesting. The Graminaceæ and Compositæ are the two most important families, the pollens of which give reactions. In the Compositæ, ragweed and goldenrod are closely related and the dandelion distantly related. If you are sensitive to one pollen you are liable to be sensitive to another closely related pollen. If you are sensitive to ragweed you will be sensitive to goldenrod, but the degree of sensitiveness may vary considerably; but you may be free from any sensitiveness to dandelion. It is like the groups reactions exhibited in animals.

It is perfectly possible to be highly susceptible to ragweed and goldenrod pollens and also to display the same sensitiveness to grasses. Occasionally we find an unfortunate individual who is sensitive to the grasses in the spring and to the autumnal pollens. If you inject such a case with pollen extracts of one of the groups to which he is sensitive, it leaves him just as sensitive to the other. As regards asthma it is interesting to note that, even if no very definite hay fever symptoms are exhibited, cases of seasonal asthma will frequently respond to treatment with specific pollens to which they are sensitive.

I want to mention the fact, too, that I believe the great majority of us are subject to sensitization phenomena. Not that everyone of us is afflicted with hay fever or asthma, but we have a lot of intestinal and other disturbances which are not fully understood, but which to judge from blood reaction are probably attributable to foreign proteins derived from foodstuffs, etc. Furthermore, there is a hereditary predisposing tendency to develop sensitization, which I consider is simply due to the fact that our protoplasm is more or less permeable, as indicated previously. These charts represent families exhibiting a predisposition to sensitization, and you see how closely analogous they are to Mendelian theories. You see the ratios in which the condition tends to occur in certain families. Owing to the prevalence of weeds, particularly ragweed and goldenrod, in Buffalo and vicinity conditions are favorable for hay-fever development, consequently many children belonging to susceptible strains develop the condition who might escape in other localities. Using the opthalmic test, the rise in resistance under treatment may be noted. But I want you to note the immediate drop in resistance afterward. The response is not permanent, but there is this to be said, that the individuals who are treated from year to year do apparently acquire finally an increased immunity.

Another important point: We may use calcium salts with great effect in certain individuals who do not react to the immune procedures, especially fat people, and that, again, fits into my theory that it is a question of the solubility of calcium salts in fat. It is a fact that calcium salts act very well with fat people and very badly with thin people, and, again, I think it is due to the permeability of the protective film.

Another point I want to bring out is that we have had some extraordinary cases of immunization. A lady came to us with hay fever. We tried her with every possible pollen and she gave no reaction. But she said that she was certain she was sensitive to flies. We collected the particular flies that she said she was susceptible to, obtained a solution after precipitation with acetone, gave her two or three injections, and she claimed she improved. At least there was a reaction, specific and not simply local—not of the skin alone but systemic.

There is occasionally a complement deviation in the blood.

The CHAIRMAN. Have you anything to add, Dr. Hitchens?

Dr. HITCHENS. I have nothing to add, Mr. Chairman, except to state that we have observed some patients who have been susceptible all the year around, and after two years' treatment have been apparently cured. We have been working on hay fever about four years and we have had 62 cases. I have forgotten just what percentage have been entirely relieved by treatment. One very interesting case susceptible to this pollen has been relieved. In our paper we have gone into the history of the problem. We have done that with a particular end in view, since most of the present-day writers are apparently ignoring the work of Blackley, and any one who will take the trouble to read his little work, published in 1873, will see that he has done all the work that one could do up to that time. Then there was very little known about the chemistry of proteins, and it remained for Dunbar to clear up the chemistry of the proteins. Active or passive immunity did not exist in the literature at that time, except, of course, in smallpox vaccination, so that all we have added since Blackley has been chemistry and active and passive immunization. So I think in our future work, before claiming originality for anything, we should be pretty familiar with Blackley.

Dr. J. BRONFENBRENNER. I happened to have a patient with an idiosyncrasy to egg white, and it was very dangerous to immunize her actively, because together with intestinal disturbance she has very severe asthma whenever the amount of antigen injected is great enough. Now, we began by injecting her with dilutions of 0.02 c. c., 1–8000, and we have come inside of two months no further

than the same amount of dilution, 1–2000—just four times as much. What is your prognosis in that case?

Dr. LYSTER. As one who is interested principally in the practical side of this subject I wish to say that I hope it will not be lost sight of completely, and that we will hear something more of the practical side of the results of Dr. Clowes's and Dr. Hitchens's work.

Dr. TOM WILLIAMS. I would like to ask Dr. Clowes if he has observed any relationship to adrenal administration in anaphylactic reactions of these people, also in regard to the giving of morphine. The reason I ask is because I have had cases in which adrenal substance has diminished this tendency and in which the taking of morphine has diminished it or caused it to cease. One man, I think, became a morphine-maniac, and when he took morphine the condition ceased.

Dr. KEBLER. I would like to ask the doctor if he has had any experience with the product containing a very small amount of cocaine which has recently been put on the market.

Dr. BROWN. I wish simply to say that in our observations we find the skin reaction entirely satisfactory, and we are rather inclined to discountenance the use of the ophthalmic reaction and think it should be eliminated entirely. We believe that in the hands of the general practitioner there may be some dangerous reactions. The skin reactions are very satisfactory, and if we find the particular protein to which the patient is susceptible we will be able to relieve all their symptoms, even though they are asthmatic.

Dr. WEIL. I would like to ask if anyone has ever had the temerity to inject any of these subjects intravenously, whether there is then the localized reaction, or whether there is a generalized reaction? Of course, if one used small amounts it would be a perfectly harmless thing. I do not know that it has ever been done. I believe injections have been done subcutaneously, and then I believe there were distinct symptoms from the injection of the antigen.

Dr. BROWN. We have injected guinea pigs subcutaneously and intraperitoneally with the idea of sensitization, and later gave 5 c. c., both doses representing 1 milligram of protein. No symptoms occurred. One of the manifestations, I might say, of the subcutaneous injection of human beings with these small doses of protein is that within 5 to 10 minutes the patients notice a distinct drying of the mucous membranes of the nose.

Dr. CLOWES. So far as I am aware I was the first to experiment with active vaccination against the autumnal form of hay fever by injecting the extracts of ragweed pollen, and I was the first individual tested. I would not for one moment suggest, of course, that I was the first to take up this general problem. There was no chance in the limited time at my disposal to talk about previous

work, with which I presumed you were well acquainted. It has been gone over very extensively by numerous investigators. The originator, of course, on a large scale, was Dunbar, followed by Wright and his pupils. We introduced the method of acetone precipitation, which has given satisfactory results. I worked up the dosage on myself and have also given myself a small intravenous injection, I am glad to say without result, but I have experienced a mild anaphylactic shock. In order to keep my experimental squad together I ran up my dose a good deal ahead of theirs and got an anaphylactic shock. I have since used that dose as the limit and have noted that a slight anaphylactic shock leads to suppression of hay fever symptoms. It is a dangerous thing to work with, so we start in with a very small dilution and work up. We have worked up to 1 c. c. of 1–1.000. We give 15 or 20 small doses at an interval of two or three days. Dunbar particularly gave up any attempt at active immunization, because he started in one of his cases with 10,000 times the dose we give, and it took him several days to pull his case through. I have tried all sorts of antigen and antibody combinations, taking my own serum and the serum of other sensitive individuals with an antigen, and tried by incubation to get anaphylatoxins and to utilize them on nonsensitive individuals with absolutely no result. I have never been able to prove anything in that way, which is, I believe, in support of Dr. Weil. With regard to drugs, I have tried morphine and other drugs with absolutely no results excpt temporary alleviation. Cocaine was mentioned. It does give a temporary alleviation; it is not a cure; can not be a cure, and simply gradually weakens resistance to the disease.

My condition five years ago had reached the point where I was incapacitated during the hay-fever season, but the last four years I have been able to carry on my work as well as I can now. Those for whom we can do nothing are generally the ones for whom we can not at present find the particular plant or protein to which they are sensitive. I do firmly believe that when we find the particular protein we shall be able to relieve them. As regards the lady Dr. Bronfenbrenner could not work on for egg white, I should advise her to keep away from egg white. If you find such difficulty in running up resistance against pollens or food proteins, then I would most undoubtedly advise the person to go to another locality or to give up the particular protein to which they are sensitive, because it is probably a question of greater permeability of the intestinal tract and mucous membranes as compared to other people.

Dr. BRONFENBRENNER. If she just goes into a drug store for a glass of soda water, drinking from a glass that has contained egg white, she develops the marked symptoms.

Dr. CLOWES. I have seen innumerable cases like that with fish, etc., where there would be urticaria and other most distressing symptoms. The high degree of sensitiveness which is developed is really extraordinary. Dr. Weil's question, as to whether a calcified brain is more permeable or less permeable, is most important. That is what old age would seem to be. In old age there is the ever-increasing effect of toxins and destructive agents upon delicate protective films, tending to break down and interefere with these films.

Calcium is mobilized to protect the film, and consequently we find increased calcium in old age, arteriosclerotic calcification in the brain, etc. It might be possible on this basis to produce a structure resembling an egg shell. I have a chart showing calcium counteracting many hundredfold the amount of caustic soda and oleate that we use in ordinary drop experiments. Whenever we have calcium deposited in huge quantities it appears to have been mobilized to counteract the destructive effect of ferments and other dispersing or destructive agents.

Dr. KEBLER. Since the doctor has brought up this question of calcium so prominently I would remind him that there has been a great deal of work done on the value of calcium compounds in the treatment of tuberculosis. Has the doctor any views on that point?

Dr. CLOWES. Simply that calcium increase may be helpful in counteracting toxic agents. Calcium may be used to advantage in counteracting conditions where increased permeability of the tissues occurs. It acts at first by promoting continuity of the film and by preventing its destruction. Ultimately calcification occurs.

The CHAIRMAN. If there is no objection the following papers will be read by title:

Seroterapia antipestosa intensiva, by José Moreno.

El asma, by J. A. Rampini.

SEROTERAPIA ANTIPESTOSA INTENSIVA (MÉTODO DE PENNA).

Por JOSÉ MORENO,

Profesor Suplente de Materia Médica y Terapia en la Facultad de Medicina, de Buenos Aires, Argentina.

I.

La peste bubónica ha sido observada por primera vez en la República Argentina al mismo tiempo que la epidemia de Oporto en 1899.

Según las investigaciones de Agote y Medina (La peste bubonique dans la République Argentine et au Paraguay, 1901), ella habría sido directamente importada por el paquete *Zeier* cuyas mercaderías infectadas fueron en parte transbordadas al vapor *Centauro* de la Carrera de Montevideo a la Asunción (Capital del Paraguay). En este vapor murieron tres tripulantes (abril de 1899).

La epidemia tomó cuerpo en la Asunción y una comisión argentina fué designada para su estudio.

Descendiendo por el Río Paraná dos focos principales se desarrollaron en los puertos más importantes de este río, Rosario y San Nicolás.

Los primeros casos en Buenos Aires fueron internados en la Casa de Aislamiento en enero de 1900. Provenían del Puerto de esta Ciudad y fueron asistidos y observados por el Dr. José Penna, profesor de clínica epidemiológica en nuestra universidad.

Con intervalos más o menos largos nuevos enfermos han sido observados y algunas epidemias se reproducen de 1905 a 1912.

Las formas clínicas más frecuentes han sido: 1°, Ganglionares: (*a*) de tipo agudo; (*b*) subagudas; (*c*) crónico. 2°, Neumónicas: (*a*) neumonias francas; (*b*) bronconeumonias. 3°, Septicémicas. 4°, Carbunculares.

II.

Mientras Calmette y Salimbeni en Oporto introdujeron en la terapia de la peste la vía endovenosa para la aplicación del suero antipestoso y duplicaban las dosis hasta entonces empleadas, Penna aplica también en Buenos Aires este método, sin conocimiento previo de la observación de aquellos cuya comunicación (Annales de l'Institut Pasteur, 1899) llegó a Buenos Aires a fines de enero de 1900).

Penna había empleado repetidas veces el método de la inyección endovenosa de diversas soluciones, práctica adquirida durante la epidemia de cólera de 1886 con los Sueros de Hayem, motivo por el cual la vía sanguínea fué también elegida por él para tratar la peste.

Pero aparte de esta coincidencia con el método de Calmette y Salimbeni, una modificación fundamental fué introducida poco después por el profesor argentino en el tratamiento de los nuevos casos de peste. Consistió ella en el aumento progresivo de las dosis de suero antipestoso por la vía venosa, hasta llegar al doble, triple y aún sextuplicar las cantidades empleadas por aquellos en una sola inyección.

Este procedimiento francamente intensivo constituye un progreso excepcional para la época, tanto más digno de mención cuanto que las observaciones posteriores en Brasil-Argentina y aún en la India actualmente confirman los éxitos de las grandes dosis. Cuando se lee la comunicación de Calmette y Salimbeni y se hace el examen de las observaciones por ellos efectuadas en Oporto es fácil convencerse de que el máximum de las dosis de suero empleadas por estos en las inyecciones endovenosas no excede de 20 c. c. en una sola vez, dosis que se repite, con excesiva prudencia en los días subsiguientes, alternadas en muchos casos con dosis subcutáneas de 40 c. c. como máximum, y que demuestran no solamente prudencia sino relativo temor al suero por vía endovenosa como lo comprueba la observación del malogrado médico Dr. Cámara Pestana fallecido allí y quien sólo en los últimos días de su grave infección recibió moderadas inyecciones por vía sanguínea.

Penna en Buenos Aires aumentó muy pronto estas dosis que Calmette llamaba "Massives" sustituyéndolas por otras intensivas primero de 70 c. c. en una sola inyección endovenosa (suero antipestoso del Instituto Pasteur) y más tarde las elevó hasta 100 y 120 c. c. del mismo suero, que se repiten sin inconveniente a las 12, 24 y 48 horas después si es que los síntomas de la infección así lo requieren.

Esta práctica de felices resultados constituye esto que llamamos en la Argentina Seroterapia intravenosa intensiva y para el que propongo la denominación de método americano de Penna.

Las observaciones primeras de este método fueron consignadas al Profesor Lignieres con el resumen en los 15 casos iniciales donde Penna escribe:

Creo que la mortalidad de 21 por ciento habría sido más reducida si desde el principio hubiera sabido manejar mejor el suero, pues posteriormente y con más experiencia he visto curar casos más graves que los que fallecieron usando el medicamento a dosis masivas-intensivas. En efecto la observación pronto me reveló que para

lograr éxito era menester como en la diftería emplear dosis suficientes en tiempo oportuno. (Carta a Lignieres, abril, 1900; Penna, Lecciones clínicas sobre la peste bubónica, 1902.)

Posteriormente y gracias a nuevos casos Penna llegó a perfeccionar su método probando la inocuidad de las altas dosis de suero.

Nosotros hemos empleado este procedimiento llegando hasta inyectar 400 c. c. en tres inyecciones con 12-24 y 48 horas de intervalo sin otra consecuencia que los pequeños fenómenos de la llamada "Enfermedad sérica de Von Pirquet" los que por otra parte sólo se observan en un número limitado de enfermos.

En lo que se refiere a los resultados nosotros hemos consignado en un trabajo sobre seroterapia antipestosa (tesis de profesorado) que las estadísticas en las epidemias americanas tratadas por este método son las que dan menor mortalidad; Chodsky en la India lo emplea (por vía subcutánea) y sobre 13,000 casos confirma los buenos efectos de las dosis intensivas. Además la observación de los casos demuestra una evolución más favorable según anotaremos en breve.

Entretanto sostenemos que la seroterapia antipestosa intensiva constituye una ampliación fundamental sobre el método masivo de Calmette y Salimbeni, que si en nada amengua la gloria de tan eminentes sabios, merece en cambio ser anotado en honor del distinguido clínico argentino Profesor Penna. Y con tanta mayor justicia cuanto que en la época en que dicha modificación fué iniciada el criterio sobre administración de sueros por vía endovenosa y aún subcutánea no era amplio como en la actualidad.

III.

En 1906 y 1912 hemos aplicado la seroterapia intravenosa intensiva a pestes ganglionares neumónicas y septicémicas y he aquí nuestras comprobaciones.

Pestes ganglionares agudas.—Nuestras observaciones se refieren a casos en todos los cuales la presencia del bacilo de Yersin ha sido revelada por el examen directo de punción de ganglios infartados o por cultivos o inoculaciones verificadas en el laboratorio del Hospital Muñiz, dirigido por el Profesor Uriarte.

En las formas agudas el principio brusco se acompaña de grandes elevaciones térmicas 40° y 41°—delirio—inyección conjunctival, estado tifoideo con infartos simples o múltiples visibles dolorosos y de tumefacción rápida. La inyección intravenosa de 100 a 120 centímetros cúbicos de suero produce casi inmediatamente una mayor elevación térmica de 1° y aún más, seguida al cabo de un breve intervalo, dos o tres horas de un descenso que llega hasta la normal 37° o cerca de ella. En muchos casos la fiebre no reaparece y la mayoría de los síntomas generales incluso el bubón se atenúan. El infarto ganglionar se resuelve a vista de ojo como decía Yersin, frase oportuna, porque en efecto hay bubones cuya tumefacción disminuye notablemente en pocas horas, por la acción del suero.

En otros casos una nueva elevación térmica, casi siempre menor que la primitiva indica la necesidad de una nueva dosis, de refuerzo observándose que efectivamente la fiebre desciende como si se tirase la temperatura hacia la normal.

Esta evolución es la más favorable; los enfermos al cabo de una o dos inyecciones de 100 a 120 c. c. de suero curan en pocos días.

En un tercer grupo el gran ascenso térmico dominado, sobrevienen nuevas temperaturas de tipo irregular con poca alteración del estado general, que producen remisiones irregulares, acompañándose este estado, con infarto doloroso, edematoso y tendencia a la supuración. El abceso ganglionar se forma y la fluctuación indica el momento de abrirlo y drenarlo siguiendo la curación como un abceso común.

En los sujetos inyectados los bubones secundarios no presentan la agudez ni la gravedad que en otros en donde el reblandecimiento de infartos antiguos llega hasta producir una septicemia pestosa aguda y la muerte, caso observado una vez en el Hospital Muñiz.

Infartos ganglionares sub-agudos y crónicos.—Las formas ganglionares subagudas se caracterizan por una defensa del organismo que resiste a la violencia inicial común y localiza la infección a los grupos ganglionares sin grave repercusión sobre el estado general. Nosotros hemos visto muchos enfermos cuya infección databa de dos y tres semanas. La temperatura en estos casos no era muy elevada (38°, 38.5°), los ganglios dolorosos, a veces edematizados y adheridos o aislados, ya con síntomas de pronta supuración o en ciertos casos duros aún.

El tratamiento lo efectuamos con el mismo método que para los anteriores. Estos casos y los del tipo crónico presentan esta particularidad que los síntomas de infección ceden fácilmente; pero el infarto es más rebelde, tienen pues, esto de paradógico, la infección más benigna, y la enfermedad más larga. Muchas veces hay que provocar la resolución o la supuración ya con los emolientes continuos o por inyección de sustancias provocadoras de leucocitosis. Hemos empleado en algunos la inyección en el ganglio de una solución de nucleinato de soda al 1/100 de 1 a 2 c. c. con la cual se provoca una supuración rápida.

Infartos crónicos.—Estas pestes ambulatorias se confunden a menudo con adenitis diversas, especialmente tuberculosas. Ellas han dado origen al estudio del llamado también "bubón climático" que para algunos autores no es sino la variedad de peste atenuada.

Nosotros las hemos observado en sujetos habitantes de regiones o locales infectados. El principio de la afección es lento, los síntomas reaccionales muy benignos. Las punciones de los ganglios dan muchas veces resultados negativos en el examen bacteriológico directo; pero insistiendo en la investigación y sobre todo con los cultivos e inoculaciones llega a encontrarse el germen pestoso. Hemos hecho referencia al peligro de un posible reblandecimiento ganglionar tardío y la aparición de una septicemia aguda. El Profesor Penna pudo observar un caso de éstos; el sujeto portador de los ganglios durante varios meses murió en el Hospital Muñiz y la autopsia confirmó el caso. Esta enseñanza determina la necesidad del tratamiento específico por el suero, aunque los síntomas clínicos sean poco intensos. Hay casos en donde el reblandecimiento ganglionar reviste el tipo necrótico cuya reparación es lenta y la cicatrización se rodea de tejidos duros leñosos. El tratamiento de la forma ganglionar crónica puede ser menos *intensivo;* nosotros hemos hecho grandes y moderadas dosis 120–100 y hasta 80 c. c. en ciertos casos intravenosas en otros subcutáneas. Aconsejamos no emplear la vía endovenosa si previamente se ha hecho la subcutánea. Pueden asimismo no repetirse con poco intervalo. A veces hacemos una inyección cada seis días hasta tres y cuatro inyecciones.

Pestes neumónicas.—Las formas clínicas observadas han sido del tipo de neumonia y bronco-neumonia. A veces los tipos septicémicos se agregan a los neumónicos con tal rapidez que es difícil determinar si la forma es primitiva o secundaria. Esta invasión sanguínea y las degeneraciones parenquimatosas agudas indican la necesidad de las inyecciones intensivas precoces y repetidas. Sólo así pueden justificarse los éxitos relativos en las epidemias sudamericanas frente a la estadística de la última epidemia de Mandchuria cuya mortalidad ha sido de 100 por 100 en las formas neumónicas.

En Brasil, Ferreyra y Tavares de Macedo, han salvado casos neumónicos de peste por las grandes inyecciones.

En Buenos Aires Penna y los médicos del Hospital de Aislamiento (Bonorino, Battaglia, Barrio, Mare, Rioja) han tratado neumonias pestosas con este método consiguiendo resultados favorables. Nosotros lo empleamos también en varios casos habidos en 1912 sin poder aun consignar estadística fija por las variables circunstancias de cada caso debidas a la gravedad de la infección que no tiene en esta forma tipos uniformes.

Argerich y Passalacqua (del Departamento Nacional de Higiene de Buenos Aires) han conseguido también éxitos parciales en una pequeña y mortífera epidemia pul-

monar que asistieron en dos localidades campestres de la provincia de Santa Fe (Argentina) en 1912.

Formas septicémicas.—Las mismas consideraciones son aplicables al tratamiento de las septicemias pestosas. Primero, por la gravedad de la infección y la acción degenerativa de la toxina; segundo, porque en muchos casos la forma aparentemente ganglionar aguda es sintomática de la infección generalizada. La inyección endovenosa intensiva y precoz puede evitar la muerte.

Formas carbunculares.—En el Hospital Muñiz se han tratado algunos casos de forma carbunclosa, con buen éxito mediante este método. Nosotros no hemos podido observar casos de esta forma.

IV.

La evolución de la seroterapia antipestosa queda confirmada por el éxito que revelan las estadísticas generales de las diversas epidemias frente a las modificaciones de los distintos métodos.

Los resultados más favorables corresponden a las epidemias americanas de Brasil y Argentina en donde sistemáticamente se emplea la seroterapia intensiva.

Chodsky en la última estadística de las epidemias de la India en que tan importante actuación ha tenido se muestra también partidario de las grandes dosis intensivas. Él prefiere la vía subcutánea e invoca para ello la facilidad y rapidez de acción. No concebimos como la vía subcutánea pueda ser más rápida que la intravenosa.

Las consecuencias de la seroterapia intravenosa intensiva no contraindican su empleo. Los accidentes séricos inmediatos son benignos y sólo se observan en número limitado de casos. Los producidos por reinyección tardía (anafilaxia) no revisten tampoco gravedad.

Nosotros hemos empleado sueros a dosis intensivas sólo hemos visto dos casos de schok anafiláctico ninguno mortal. Uno de ellos con suero antitetánico(dosis intravenosa intensiva, método de Penna) y otro con suero normal de caballo dosis moderadas de 10 c. c. En ambos el empleo de la vía intravenosa después de haber empleado la vía subcutánea fué la causa del accidente. La reinyección en el segundo caso fué a las tres horas de la inyección anterior, el sujeto había recibido antes 29 inyecciones de suero de caballo en siete meses con intervalos breves de varios días (caso de hemofilia).

Expuesto someramente lo que antecede nos creemos autorizados a anotar las estadísticas y conclusiones que siguen:

Estadística comparada de las diversas epidemias de peste tratadas con los diferentes métodos:

PRIMER PERÍODO.—*Método de Yersin: Inyecciones subcutáneas de suero de 10 a 20 c. c.*

Autores.	Epidemias.	Años.	Enfermos tratados.	Muertos.	Mortalidad.
					Por ciento.
Yersin	Canton y Amoy	1896	26	2	7.6
	Bombay	1897	50	17	34.0
	NaFrhang	1898	33	14	42.0
Simond	Maudvi	1896	136	89	65.0
	Bombay	1896	171	99	57.0
	Mountra	1896			
	Kuratchi	1898	75	37	49.3
Zabolotny	Mongolia, Forma neumónica	1898	16	12	75.0
Delay	Montsé (China)	1898	10	4	40.0
Thiroux	Tamatave	1896	20	11	55.0

SEGUNDO PERÍODO.—*Método de Calmette y Salmibeni: Inyecciones Intravenosas de 10 a 20 c. c. alternadas con inyecciones subcutáneas de 20 a 40 c. c.*

Autores.	Epidemias.	Año.	Enfermos.	Muertos.	Mortalidad.
					Por ciento.
Calmette y Salmibeni	Oporto	1899	142	21	14.7
Metin	Oporto	1899	6	1	16.6
Primet	Numea	1899–1900	7	2	28.5
Noe	Numea	1901	17	8	46.9
Oswaldo Cruz	Rio Janeiro	1900–1901	278	99	35.6
Agote Medina	Rosario (Argentina)	1900	26	11	42.0
Clarac	Guafunga	1902	71	32	45.0
Ruffiandis	Ton Techow	1902	67	34	50.0
	Tonkin	1903	72	42	58.3

TERCER PERÍODO.—*Método americano de Penna: Inyecciones Intensivas de 70 a 120 c. c. por vía endovenosa y subcutáneas repetidas.*

Autores.	Epidemias.	Años.	Enfermos.	Muertos.	Mortalidad.
					Por ciento.
Penna	Buenos Aires	1900–1905	204	28	14.2
Duprat	Río Grande, Método subcutáneo-intensivo.	1902	45	7	15.5
Hospital Paula Cándido	Río de Janeiro (Brasil)	1902	268	68	25.6
		1903	541	124	22.9
		1904	504	103	20.4
		1905	149	25	16.5
Hospital San Sebastián	Rio Janeiro	1905	138	30	21.7
		1906	187	54	28.8
Tavares de Macedo	Campos (Brasil)	1906	14	2	14.0
Antonino Ferrari	Rio Janeiro	.....	69	5	7.6
		.....	21	8	[1] 38.0
		.....	11	2	18.0
Hospital Muñiz	Buenos Aires	1905	41	4	9.0
		1906	94	22	23.0
		1907	125	15	12.0
		1908	60	7	11.0
		1909	93	14	15.0
		1910	47	7	15.0
		1911	76	9	11.0
		1912	68	5	7.3

[1] Subcutáneo.

CONCLUSIONES.

1ª. La práctica de la seroterapia antipestosa ha demostrado la necesidad del aumento intensivo en las dosis de suero.

2ª. Las inyecciones intravenosas deben considerarse de especial importancia por la rapidez de su acción que es un elemento necesario en el tratamiento especialmente de las formas agudas.

3ª. El método de las dosis intensivas debe considerarse una modificación fundamental comparado con el de las dosis masiva de Calmette.

4ª. Esta modificación debe ser denominada método americano de Penna.

5ª. Las estadísticas mundiales demuestran que el mejor tratamiento de la peste bubónica lo constituye el Método Intravenoso Intensivo de Penna.

EL ASMA; SUS CAUSAS, DEFECTOS E INCONVENIENTES DE UN SOLO MÉTODO EXCLUSIVO PARA CURARLA COMO EL MÉTODO DE EFRAIM. NECESIDAD DE VARIOS TRATAMIENTOS CON RELACIÓN A LAS VARIAS CAUSAS ASMATÓGENAS.

Por JOSÉ A. RAMPINI.
Montevideo, Uruguay.

Durante diez años de clínica asmática que vengo haciendo con mis enfermos he estudiado diversos casos de asma, especialidad a la cual me dedico y he llegado a las siguientes conclusiones que oportunamente ampliaré.

El asma no es una enfermedad, sino un síndrome, es decir que los asmáticos no son todos iguales, pues hay diversos tipos de asmáticos.

Además del árbol respiratorio, los órganos más diversos pueden producir asma: el estómago, el hígado, el intestino, el útero, los ovarios, el riñón, el aparato circulatorio pueden producir asma todos los caracteres del asma verdadera, típica.

Se cita un reflejo hepato-nasal que puede producir asma nasal sin que haya nada en la nariz.

He visto un cólico hepático con todos los caracteres del asma pulmonar.

He visto un caso de embarazo de dos meses complicado con accesos de asma que no cedieron a pesar de haber empleado los calmantes usuales que tan buenos resultados me dieron en otros casos. Sospechando que el asma fuera producida o por lo menos desempeñara un papel importante en su producción la intoxicación, por insuficiencia ovárica hice a la enferma varias inyecciones de ovocitina Aster fresca y obtuve un excelente resultado. Continué este tratamiento durante todo el embarazo con el mismo resultado.

He visto un caso de asma con bronquitis catarral en un sifilítico terciario, y los accesos de asma y la bronquitis curaron con el tratamiento mercurial.

Esto demuestra que la patología del asma es más complicada de lo que a primera vista parece y que cada asmático debe ser estudiado detenidamente. Para conocer bien el asma es necesario conocer bien la patología de todos los órganos y el tratamiento debe variar según los casos.

Dr. José Moreno, profesor suplente de la facultad de medicina de Buenos Aires, submits the following "Relación sintética de los trabajos presentados (por él) al Congreso."

Trabajos presentados al Congreso Panamericano de Wáshington:

Primer trabajo: Seroterapia antipestosa intensiva (método americano de Penna).

Estudia el autor el origen de los casos de peste bubónica en la República Argentina desde su primera aparición en 1900 hasta la fecha. En diversas epidemias de 1905–6 y 12 a formas ganglionares y neumónicas ha empleado las inyecciones de suero antipestoso por vía intravenosa siguiendo el método del Profesor Penna de Buenos Aires consistente en el empleo de dosis intravenosas de 100 y 120 c. c. de suero del Instituto Pasteur. La primera inyección que puede ser de 120 c. c. es seguida a las 24 o 48 horas de una segunda de 100 c. c. con lo que se obtiene un rápido descenso de las curvas febriles y los síntomas de la intoxicación pestosa se atenúan rápidamente en algunos casos de forma ganglionar.

El estudio de los casos publicados por Calmette y Salimbeni en la epidemia de Oporto en 1899 demuestra que las dosis intravenosas de 20 c. c. empleadas por estos observadores en aquella epidemia y a las que denominan dosis masivas son insuficientes como se observa en la persistencia de los fenómenos febriles durante 24 horas mientras que por el método de Penna con dosis intensivos de 100 c. c. endovenosas los descensos térmicos son muy rápidos a veces desde las primeras horas que siguen a la primera inyección. El autor propone denominar este método seroterapia intra

venosa intensiva o método americano de Penna, para diferenciarlo de la denominación "masiva" o método de Calmette.

Para mayores detalles ver su comunicación y su tesis actualmente en mpresión (Seroterapia de la peste bubónica. Imprenta de la Semana Médica Argentina, Buenos Aires, 1915) conteniendo el estudio comparativo con numerosas observaciones y la comunicación a este Congreso.

Segundo trabajo: Climatología médica; estaciones invernales argentinas.

El autor estudia la región argentina situada al norte del 31° de latitud y este del 61° de longitud en las proximidades del Paraguay. El estudio climatológico demuestra la uniformidad climatérica apta para la fundación de Ciudades Invernales, su gran similitud con los climas invernales europeos y la conveniencia de la creación de residencias higiénicas, secas y húmedas. Las proximidades del Río Paraná y de las zonas de grandes bosques de la región subtropical facilitan la humedad atmosférica para el equilibrio de las temperaturas y la moderación en la velocidad de los vientos. Estos factores unidos a la belleza del suelo, a la latitud pureza de aire hacen que estas zonas posean un clima suave, uniforme, semejante al que Lindsay estudió en las llanuras de Australia, en idéntica latitud y que preconizó para la tuberculosis. El autor considera que las formas créticas y hemoptoicas son beneficiadas, mas aún que en las zonas de Montaña. Su estudio data de 1909 y se anticipa así a la noción de climas complementarios que constituye en la actualidad la última palabra en cuestiones de climatoterapia. A él se debe la fundación de una primera residencia invernal llamada "Ciudad de Invierno."

Tercer trabajo: Sobre transformaciones que sufre el "606" en el organismo.

Sin ser un trabajo experimental, el autor, sometido al desarrollo de este tema, como prueba oral, para el profesorado universitario, en un término breve, raciocina sobre la quimioterapia del "606" y apoyándose en la fórmula de constitución del salvarsan, en las experiencias hechas en el servicio de Jeanselme en París, en los hechos clínicos sostiene que debemos aceptar "que el edificio molecular del "606", una vez introducido este cuerpo al organismo, se derrumba dejando el arsénico libre, el que en su mayor parte es eliminado, otra parte fijada en el organismo los átomos amidados serían transformados en el hígado y los oxidrilos, con función fenólica eliminados por la orina. No existiendo bibliografía sobre el tema, el autor expone su doctrina a la consideración del congreso.

Cuarto trabajo: Pseudo-tuberculosis pulmonar cocobacilar; tesis de doctorado.

El autor estudia varios casos clínicos en donde afecciones pulmonares con síntomas de tuberculosis pulmonar, sin bacilos de Koch han presentado en los esputos y aun en cortes histológicos masas zoogleicas con los caracteres morfológicos-culturales y de inoculación del cocobacilo de la pseudo-tuberculosis zoogleica de Malassez y Vignal. Es el primer trabajo, conjuntamente con una observación del médico argentino Mario Acevedo, en que se establece en el pulmón humano la existencia de nódulos de reacción al cocobacilo de Malassez, por lo que el autor cree en la posibilidad de confusiones de diagnóstico clínico, con reacciones negativas a la tuberculina, en los casos de bronco-neumonias crónicas y esclerosis pulmonares. Las investigaciones bacteriológicas y anátomo-patológicas rigurosas podrían aclarar la frecuencia de tales pseudo-tuberculosis pulmonares.

Quinto trabajo: Caso de tachipnea histérica simulando "coup de chaleur."

Estudia un caso de histeria en donde la enferma, joven de 18 años simula "coup de chaleur" durante una época de fuertes calores. Se caracterizaba por congestión y cianosis de la cara, dispnea intensa con movimientos respiratorios aparentes hasta 130 por minuto. El autor observa que contra las descripciones habituales de la tachipnea el ritmo respiratorio no es regular, sino que aparece así por la rapidez de los movimientos y que un hábil juego respiratorio permite acumular aire para dar lugar a una serie de expiraciones cortas. Además en la tachipnea de este caso nota los esfuerzos

aparentes de la enferma para simular el ahogo. Considera de interés el caso clínico, por no encontrar en la tachipnea descrita por los autores, la simulación del "coup de chaleur."

Sexto trabajo: Hemofilia familiar de tipo hemoptoico sistemático.

Caso clínico en donde la herencia hemofílica es doble. El enfermo a quien estudia con todo detalle, para excluir confusiones de diagnóstico, ha llegado a perder hasta 14 litros de sangre en un período de cinco meses.

Las circunstancias propias del caso le permiten creer en que de las teorías hemofílicas es más probable la perturbación de los órganos hematopoieticos que suministran una sangre anormal por poussées. Tiene además interés por haber observado un "shock" anafiláctico sérico después de 29 inyecciones de suero normal de caballo y motivado por el cambio en la vía de introducción del suero. Las inyecciones anteriores habían sido subcutáneas, la última tres horas antes de la endovenosa que fué practicada por un colega llamado urgentemente. El "shock" anafiláctico no tuvo consecuencia grave.

Séptimo trabajo: Batallones escolares, educación física.

Estudio presentado al primer congreso nacional del Niño en la República Argentina. Se denominan así agrupaciones de niños de la Sociedad Sportiva Argentina. A pesar de su nombre los batallones escolares no encierran concepto de militarización infantil, sino de agrupación con fines de educación física, como puede verse en las fotografías respectivas. Estudia el origen y caracteres del niño argentino y la necesidad de graduar los ejercicios progresivamente empezando por la gimnasia sueca antes de llegar a los deportes que son la gimnasia de síntesis. Combate la gimnasia durante o después de las horas escolares por el surmenage físico que el trabajo intelectual acarrea, según demuestran los trazados con el ergógrafo de Mosso y preconiza los ejercicios al aire libre las fichas individuales del índice torácico terminando con la importancia en la higiene y hominicultura de las asociaciones de educación física racional.

Octavo trabajo: Antisepsia digestiva y bacterio-terapia.

Se ocupa el autor del origen de las infecciones y autointoxicaciones gastro-intestinales de niños y adultos, los estudios de Fisher y Langenheim sobre descomposición de albuminoides, la necesidad de tener presente en la normalidad de los procesos digestivos los estudios de Pawloff para explicar las autointoxicaciones por deficiencias secretorias, la relatividad de la antisepsia medicamentosa la importancia de la bacterioterapia láctica de Metchnicoff; pero hace notar que las preparaciones tituladas de bacterios lácticos son frecuentemente estériles por lo que preconiza el empleo de las leches fermentadas recientemente.

Noveno trabajo: Perversión moral (locura moral adquirida de Kraft-Ebing y Schüle) de origen Bassedowiano.

En un informe médico-legal, el autor establece el diagnóstico de perversión moral (locura moral adquirida de Kraft-Ebing y Schüle) en una enferma de mal de Bassedow.

Se trata de una Bassedowiana confirmada en período avanzado, con una fuerte herencia demencial, la que con toda premeditación instiga la muerte de su esposo ofreciendo dinero a los asesinos. La trama del delito revela una premeditación larga. El autor estudia la esfera intelectual y moral de la procesada, comprobando que además de la enfermedad de Bassedow y su neurosis, la enferma en cuestión presenta las características de una locura moral que aparece en ella concomitantemente con la enfermedad de Bassedow. Siendo la locura moral verdadera congénita, el autor establece que los síntomas corresponden a las perversiones morales que Ballet considera episodios de afecciones mentales y Kraft-Ebing y Schüle denominan locuras morales adquiridas.

El autor determina la irresponsabilidad de la enferma basado en que de acuerdo con André Thomas "las perturbaciones de la emotividad constituyen el fundamento de la

perversión instintiva " y la enfermedad de Bassedow es ante todo una afección que altera esencialmente la emotividad. Es el primer caso descrito en la bibliografía corriente de delincuencia premeditada y jactancia del delito en el curso de una enfermedad de Bassedow en donde en general los delincuentes lo son en forma impulsiva y transitoria.

Décimo trabajo: Presenta a la consideración del congreso varios ejemplares de lecciones de terapia higiénica y conferencia inaugural de un curso libre en el Centro de Estudiantes de Medicina de Buenos Aires, independiente de la enseñanza oficial. Lecciones de síntesis sobre temas de terapéutica higiénica, entre ellos un estudio sintético de aguas minerales, en especial de la República Argentina en donde se cumple la teoría de Gautier sobre la distribución geográfica de las aguas minerales de origen profundo en las regiones volcánicas. Muestra asimismo la existencia de todas las variedades de aguas minerales en la Argentina y fuentes termales en las más altas temperaturas existentes en la región andina.

Estas lecciones darán ideas sobre la generalización de la docencia libre incipiente aún en el país.

The CHAIRMAN. Before adjournment I beg to state that a copy of the following printed book has been presented, through the courtesy of the writer, to the Scientific Congress and is herewith reported by section VIII: Las Glándulas supra-renales en el embarazo normal y patológico, por el Dr. Juan A. Gabastou. Las Ciencias, Libreria y Casa Editora de A. Guidi Buffarini, Buenos Aires, 1915.

Adjourned at 2 o'clock.

GENERAL SESSION OF SECTION VIII.

NEW EBBITT HOTEL,
Wednesday night, January 5, 1916.

Chairman, JOHN VAN R. HOFF.

The session was called to order at 8 o'clock by the chairman.

The CHAIRMAN. The meeting will please come to order. Before proceeding with the regular program for to-night I will ask Dr. Guiteras to read by title several papers that have been submitted to the section by Dr. Genaro Giacobini, of Buenos Aires. These papers will not be read in extenso.

Hereupon Dr. Guiteras read the titles of these brief papers. The conclusions of two of these papers, previously printed, together with the author's general introduction, follow:

El que abajo suscribe, presenta a la consideración del 2° Congreso Científico Panamericano a reunirse en Washington en Diciembre de 1915 las siguientes conclusiones del:

Estudio de la pneumonia en la infancia:

1°. Existe un signo de dolor colítico en la pneumonia de la infancia, signo de dolor espontáneo o palpitatorio de la región abdominal correspondiente al colon con predominio del lado derecho y que se continúa en la intersección o ángulo que forma el colon ascendente con el transverso, dolor abdominal que no corresponde al punto apendicular descrito por Massolongo y clasificado con la denominación de "pseudoapendicitis pneumónica de Massolongo," por el Congreso Italiano de Pediatria de 1901.

2°. En la evolución hacia la curación de la enfermedad el dolor colítico desaparece antes que el dolor del costado torácico, cuando ambos se presentan al cuadro de la corroboración diagnóstica.

3°. El punto doloroso colítico de la pneumonia en la infancia, puede presentarse sin el dolor torácico.

Examen anatómico comparativo del sistema nervioso en la escala animal:

1°. La jerarquia psiquica de los animales en general es concordante con una mayor o menor reconcentración central del sistema nervioso, es decir, con el mayor o menor volumen relativo del cerebro comparado a la médula y nervios del sistema.

2°. La especie humana está regida por la misma ley de la filogenia que gobierna el conjunto del escalafón zoológico. Su potencia psiquica crece y su reconcentración central o cerebral va en aumento.

En consecuencia si estableezco una fracción, a/b, cuyo numerador represente el cerebro, exponente del de la especie humana en la actualidad y el denominador a la médula y nervios, deduciré el aumento progresivo del primero con respecto al segundo, a medida que la vida de la especie humana ascienda en poder psiquico ax/b.

La ontogenia del hombre no viola la ley establecida, pues no es más que una modalidad de la vida de la especie, así como ésta lo es del conjunto animal.

3°. Las leyes que las gobiernan son consecuencias del principio filosófico de la vida.

The remaining papers of Dr. Giacobini, submitted in manuscript, are herewith printed, together with the author's recommendations:

Los alienados delincuentes y los delincuentes alienados—Creación de manicomios criminales:

El concepto de la delincuencia del alienado es la resultante de la interpretación jurídica de los actos del mismo en función con las leyes que rigen nuestras actividades

sociales con sus preceptos y normas de conducta individual que le exigen la civilización para responder a la ética de los tiempos, y en función de la psiquiatria el alienado que tiene tendencias al delito es una entidad que lo especifica, que lo caracteriza, que le da un carácter peculiar dentro de las modalidades psicológicas de los alienados comunes. Siendo la idiosincracia del alienado delincuente tender a los actos delictuosos dentro de las reglas de un determinismo psicológico, ¿por qué negarle esa especificidad? ¿porqué no particularizarle dentro de las conquistas grandes de la psiquiatria las reglas determinantes de una conciencia que siente dentro del ritmo de sus actos extra sociales una tendencia instintiva a las leyes que rigen la individualidad en la sociedad y la civilización?

Clasificado el alienado delincuente, como un temperamento dentro de la carátula del desequilibrado mental, ¿no es por acaso particularizarle y clasificarle de los comunes alienados que estudia la psiquiatria?

La locura criminal como entidad autónoma dentro de la taxonomía psiquiátrica no existe.

La ciencia psiquiátrica no ha hecho la clasificación aún.

Sostener que un acto delictuoso cometido por un alienado en un momento de paroxismo de locura sin darle la particularidad propia y específica de locura delictuosa, sea un error, no justifica que así se califique la tendencia instintiva, repetida, hacia los actos delictuosos que particularizan y clasifican a los alienados delincuentes y a los delincuentes alienados cuyas diferencias dependen por la razón cronológica de que el estallido de la locura sea anterior en los primeros y posterior en los segundos.

En cuanto a la jurisdicción de los encargados en velar por la seguridad social, entran a participar el médico y el jurisconsulto, desde que en sus actos el delincuente necesita la intervención facultativa para el estudio diagnóstico de los procesos cerebrales del alienado, y para la terapia del mismo, y la del jurisconsulto como tutor y salvaguardia de las leyes depositarias de la defensa legal de la sociedad, desde que los alienados delincuentes y los delincuentes alienados han infrigido con sus actos una ley codificada del derecho, su acto extra-legal ha inflingido un daño de una manera dinámica en acción violatoria de la ley; distinguiéndole del alienado común no delincuente desde que sus actos, aunque muchas veces en latencias, no han infringido en el hecho las leyes del código escrito de la jurisprudencia, y con el perjuicio social correspondiente.

Dentro del movimiento filosófico y científico de la época, en que los conocimientos humanos tienden a la especialización, los estudios de la psicoantropología, médico-legales y jurídicos, deben tender a ese movimiento general de la ciencia y el saber y la creación de manicomios criminales es un desideratum que responde a esa tendencia del espíritu de la época y de la civilización.

Si fué dable refutársele a Lombroso, en lo que respecta a la característica que definió al loco delincuente, considerándolo por su espíritu de asociación y su espíritu de rebelión, con la clásica frase "la folie c'est l'isoloir de l'âme," porqué no aceptar el distingo de una modalidad clínica especial del alienado delincuente desde que sus actos se inclinan preferentemente a la acción delictuosa y a la violación de las reglas de la ley protectora de la ley jurídica y moral de las sociedades.

En consecuencia debe aceptarse científicamente la creación de institutos especiales, de manicomios criminales para el tratamiento facultativo y racional del alienado delincuente y como previsión y de defensa social.

Basado en estas consideraciones:

I. El Segundo Congreso Científico Panamericano, reunido en Wáshington en diciembre de 1915, patrocina la creación de manicomios criminales en las naciones americanas, para el tratamiento facultativo y racional, previsión y defensa social del alienado delincuente, y como un desideratum de la medicina legal y de la psicoantropología criminal contemporánea.

Creación de tribunales para niños:

Entre los problemas trascendentales de la jurisprudencia de los pueblos contemporáneos, se define grandiosa la obra de la redención moral del niño, por una sabia legislación previsora del delito.

El desenvolvimiento de los factores que tienden a la extirpación de las tendencias delictuosas de la niñez es elevar a las más altas cincelaciones del ideal humano y redimirla de los instintos inferiores de la especie.

Consecuente con las ideas de regeneración y profilaxia social de la delincuencia, urge considerar el problema de la niñez desvalida, y la creación de tribunales para niños en los países americanos, salvaguarda en parte la deficiencia del medio de vida de esos seres abandonados al acaso en los embates del vicio y la corrupción, inclinándolos al medio purificador de los métodos del trabajo y de la escuela.

Y es que respecto a las relaciones de la codificación civil americana con los menores delincuentes debería modificarse la legislación en el sentido de quitarles a los padres el derecho de la patria potestad para los menores delincuentes recidivistas y otorgar dicha atribución legal al Estado que velaría por la moralización del adolescente. La función social de la regeneración tendría toda la característica de una disciplina pedagógica-represiva adoptada a los principios científicos, bajos los auspicios y fiscalización de los poderes públicos amparados y sostenidos por la ley.

El niño educado en una ética purificada es un ente que pugna contra los medios corruptores y delictuosos, es una poderosa fuerza de hegemonía moral, vigor y dinámica activa que prepara para lo futuro la vitalidad misma de la sociedad humana en el incesante torbellino de sus evoluciones.

Los países sajones han tributado al problema del estudio y de la terapia de la criminalidad infantil el esfuerzo del espíritu práctico que los caracteriza.

Y al fundar y en la creación de tribunales para niños han querido hacer sentar, y reposar la jurisprudencia en el criterio de la libertad vigilada y que debe ser la orientación esencial de nuestra iniciativa siempre entendida bajo el contralor de las escuelas de enmiendas que funcionan en la actualidad en la Gran Bretaña para la corrección de la infancia delictuosa. La penalidad del niño desviado por la senda del delito ha sido la preocupación de los estadistas sajones como medio de previsión, corrección y enmienda, pudiendo hacer reposar el mecanismo de la represión en estos principios:

1°. Someterle a la vigilancia.

2°. Libertarle con promesa de enmienda.

3°. Enviarle a una escuela industrial.

4°. Enviarle a una escuela de reforma.

5°. Multas equivalentes al daño causado y hacer responsables de la infracción a los padres o tutores.

6°. Condenar a los padres o garantizar su buena conducta.

7°. Enviarle a un lugar de atención reglamentado legalmente.

Y preconizar en los países americanos la creación de escuelas de enmiendas, divididas en tres categorías: (1) Para la corrección, industriales para niños desgraciados o abandonados y delincuentes menores de 12 años; (2) las de reforma, para los delincuentes especiales de 2 a 16 años; y (3) las escuelas especiales a semejanza de las de Borstal para los de 16 a 21 años. La acción y misión de estas escuelas patrocinarían la misión del tribunal para niños y serían complementarias del espíritu y fondo de esa corporación.

Y en consecuencia.

I. El Segundo Congreso Científico Panamericano, reunido en Wáshington en diciembre de 1915, patrocina la reforma de la legislación penal y la creación de tribunales para niños en las naciones americanas, y en el concepto de previsión, corrección y enmienda, hace reposar el mecanismo de la represión del niño delincuente en los siguientes principios;

1°. Someterle a la vigilancia.

2°. Libertarle con promesa de enmienda.-

3°. Enviarle a una escuela industrial.
4°. Enviarle a una escuela de reforma.
5°. Multa equivalente al daño causado y hacer responsables de la infracción a los padres o tutores.
6°. Condenar a los padres a garantir su buena conducta.
7°. Enviarle a un lugar de atención reglamentado legalmente.

II. Preconiza la creación en los países americanos de escuelas de enmiendas divididas en tres categorías.
1°. Para corrección (escuelas industriales para niños desgraciados o abandonados y delincuentes menores de 12 años).
2°. Para reforma (escuelas para los niños delincuentes menores de 12 a 16 años).
3°. Especiales (escuelas a semejanza de las de Borstal para los delincuentes menores de 16 a 21 años).

Educación física, moral e intelectual del niño, según la ciencia psicológica contemporánea:

Entre los puntos de capital importancia en las que pudieran plantearse en las cuestiones científicas respecto al problema infantil, surge el enunciado de la educación del niño en todos sus factores, en todas sus modalidades de la educación física, moral e intelectual. No es posible desde el punto de vista de las verdades de la ciencia, separar en autonomía, esos distintos atributos de la actividad individual.

El niño al ser lanzado a la vida, con todos los atributos de la existencia, lleva en su ser concentrado en estado latente todas las expresiones de las modalidades que el medio deberán estimular para dinamizarlas en el ritmo evolucionado de la existencia.

La educación física del niño, debe preocupar la atención de los hombres estudiosos. El niño es un ente en plena evolución y manifestación de desenvolvimiento orgánico y psíquico.

Sus órganos lanzados a la ardua complexidad del mecanismo de la existencia, dirigen, elaboran, matizan y ritman sus palancas dinámicas en la armonización completa de la unidad del ser en el conjunto de la vitalidad.

Y en el acrecentamiento, y en la vigorización, en la solidaridad y la armonía de todos estos resortes del organismo, para el engranaje funcional de todos sus órganos para la marcha perfecta, integral y fisiológica del conjunto del ser está el verdadero concepto del cultivo de las facultades físicas en que reposa. Como veremos luego el conjunto de las modalidades morales e intelectivas que se desprenden lógica y naturalmente de esos factores naturales. El cultivo de la energía física, deberá por lo tanto estimular en una especie de euforia vital, que invite al psiquismo del pequeño ser a obrar en la vida con todos los entusiasmos y placeres de la existencia para que esos mismos atributos de la sensibilidad del alma, refluyan sobre el ejercicio armonioso del conjunto físico vigorizando la dinámica funcional de la vida vegetativa y de relación del niño.

El ejercicio metódico, en el que participan en el estímulo los distintos órganos de la individualidad física sin violencias ni brusquedades, oxigenan el campo energético de la vida, metabolizan los tejidos en la vivificación de las reparaciones orgánicas y sientan el jalón luminoso a cuyo resplandor la pedagogía puede y debe velar por la constitucionalidad moral e intelectual. Sobre esa base física, eduquemos al niño en su ética, con el sano ejemplo, con las buenas costumbres, honestidad y la satisfacción del bien cumplido.

En la psiquis del niño predomina el espíritu de imitación, de donde se desprende evidentemente que las atenciones pedagógicas que a la infancia se le debe un gran atributo, un gran factor debe considerarse en ese sentido y elevar a la sugestión infantil, la impresión de los actos lícitos y éticos que consagra la civilización y el progreso de las costumbres.

Y en consecuencia:

1°. El Segundo Congreso Científico Panamericano, reunido en Wáshington en diciembre de 1915, insinúa a las autoridades educacionales de los Estados americanos, la conveniencia científica y social de educar al niño integral y armónicamente en todas sus facultades de la actividad física, moral e intelectual.

2°. Por la educación física como medio de perfeccionamiento y desarrollo orgánico de sus elementos vitales de la existencia física, en el ejercicio metódico, racional y disciplinado de sus órganos.

3°. Por el cultivo de los principios éticos asimilados al niño por la sabia explicación objetiva del ejemplo y de los sanos principios y costumbres.

4°. Por el cultivo integral de sus facultades intelectuales por la objetividad de las cosas y principios, sin prejuicios ni sectarismos y con método pedagógico positivo y de utilidad práctica.

La heredo amoralidad infantil y su influencia social pedagógica. Higiene alimenticia del niño:

El niño, es un exponente de las idiosincracias de las aptitudes morales, intelectivas y sensitivas de sus progenitores en la evolución psíquica y filosófica que le determinan el medio ambiente en donde reposa la incubadora ética del desarrollo dinámico de las facultades integrales de la infancia.

Para el estudio ético y de su influencia social pedagógica, debemos considerar el agente individual como factor exponente de la idiosincracia propia de la raza en cuyo modelo bebe la savia fluidificante y reparadora de sus metabolismos de la vida de relación y la complexidad de ese medio en las múltiples fases de su vitalidad que crean, dirigen, neutralizan infinitas veces las disposiciones innatas de la estructura y funcionamiento individual.

La moral del niño, hereda de sus antepasados, las aptitudes del aprendizaje, evolución y perfección, la enseñanza coordina las tendencias éticas e intelectivas y las expresan con las cincelaciones de la ciencia pedagógica en la continua ascensión del ser humano hacia las regiones puras de la razón fundamental de la existencia.

La amoralidad en la infancia es el resultado de una violación, de una desorientación, de un desequilibrio del factor ético-filosófico, y en esta enunciación la heredo amoralidad infantil, abre un gran capítulo de estudio en la patología de la psicología morbosa del niño.

Se me negará rotundamente que exista el factor herencia de la amoralidad en la infancia. No pretendo entrar en una disquisición puramente teórica; pero sí admito que si bien no existe una herencia de la amoralidad, de una imperfección de la ética por deficiencia similar en sus progenitores, como semejante comprobamos en el problema de la herencia de la tuberculosis de los padres a los hijos, no obstante, las aptitudes del mecanismo psíquico-ético se hallan con inversión dinámica adaptada a desenvolverse por la senda de lo malsano y antimoral si una fuerza de pulimento ético no viene a inhibirle en el surco generoso y bello de las buenas costumbres y de los buenos principios de la vida de relación.

A la consideración del problema en cuestión, hemos planteado la influencia evidente del medio, del agente individual del niño, de su herencia psíquica-ética, y como premisa se desprende, la herencia orgánica del ser infantil de sus progenitores, copiando su estructural constitución de la existencia. Los múltiples factores que explican los fenómenos patológicos de los actos sociales, podríamos llevarlos a la consideración de los que enuncian y consideran los de la infancia. El factor económico, el estado intelectivo de una comarca o población que guía y dirige la aplicación inmediata a la solución y consideración de los problemas de la existencia.

Disciplinar el medio en el que se desenvuelve las acciones del niño, facilitando todo los resortes y recursos de la pedagogía científica para que las facultades del mismo se desarrollen en la plena y libre expansión de un campo embellecido en las galanuras de la moralidad y de los principios inmanentes de los actos de la justicia.

Para tal fin, el niño deberá recibir el nutrimento fisiológico indispensable para que las asimilaciones orgánicas se hagan de acuerdo con las leyes fisiológicas que rigen los organismos vivientes en las plenas expresiones y manifestaciones de la salud. Esta enunciación nos lleva a la consideración de un otro problema, cual el de la higiene alimenticia del niño, capítulo de trascendental importancia para el estudio de la evolución y desarrollo físico.

Desde los primeros años de la vida, alimentar a un pequeño ser, es un problema de ciencia pediátrica, que se simplifica cuando el fluido materno, la sangre de la madre, basta para dotar al pequeño niño la asimilación de esas necesidades materiales, pero si

ese recurso de la naturaleza sabia y providencial no existe, el niño peligra su alimentación en las zozobras de un nutrimento antifisiológico, deficiente y malsano.

Resolver el complicado problema de la dietética infantil, es solucionar un problema trascendental de la salud pública, puesto que se disminuye con tal cosa el porcentaje de la mortandad infantil, y paralelamente la infancia protegida por la ciencia pediátrica y de las leyes de la alimentación racional, seguirá un desarrollo de evolución física, con vigor, energía y salud, creando una adolescencia fortalecida y apta para resistir a los embates de la enfermedad y de los múltiples y complejos factores sociales y naturales que predisponen también a las acciones delictuosas.

En conclusión: 1°. Debe el estado velar por el cumplimiento de las leyes pedagógicas y racionales que se oponen al desarrollo de la amoralidad en la infancia.

2°. Extender su acción protectora en el sentido de una amplia consagración de la moral en los actos que se desprenden de la voluntad y actividad del niño.

3°. Vigilar y difundir los preceptos científicos destinados a iluminar al pueblo en el sentido de una dedicación racional y científica de la higiene alimenticia del niño.

4°. Con el cumplimiento de los enunciados resolverá ventajosamente la profilaxia de la delincuencia en la infancia.

Y con el tercer aserto escribirá el gran capítulo de la higiene física del niño y evitará la crecida mortandad en la misma.

Y en consecuencia:

1°. El Segundo Congreso Científico Panamericano, reunido en Wáshington en diciembre de 1915, invita a los Estados americanos a que reglamenten y velen por el cumplimiento de las leyes pedagógicas y racionales que se oponen al desarrollo de la amoralidad en la infancia.

2°. Insinúa a los cuerpos escolares de los Estados americanos, la indicación de intensificar la enseñanza de la moral en el niño como medio de evitar el vicio y la corrupción de las costumbres.

3°. Invita a los Estados americanos a que complementen su acción oficial en ese sentido, por su actuación extraescolar por intermedio del folleto, la conferencia pública y otros medios explicativos y de alcance popular.

4°. Invita a los Estados americanos a que reglamenten, vigilen y difundan los preceptos científicos destinados a iluminar al pueblo en el sentido de una dedicación racional y científica de la higiene alimenticia del niño.

5°. Harán práctica esta última proposición por los medios indicados en la proposición tercera.

La delincuencia y el crimen, su represión científica:

En la evolución de la jurisprudencia, en el derecho de reprimir los actos que atentaban con las leyes del consorcio colectivo, en que reposa la estabilidad de la vida del conjunto social, el espíritu penal ha ido fluctuando en las innumerables teorías y transiciones del espíritu filosófico y científico del linaje humano al través de su historia. Observada la aurora, los primeros albores del derecho codificado en función a las leyes de la penalidad se transparenta diáfana a la concepción e interpretación histórica, la base movediza en que reposaba el concepto de la reprensión del acto delictuoso, cuando aún se hallaban los estudios y los conocimientos biológicos en una evidente ruta rudimentaria en la evolución incesante del espíritu científico hacia el conocimiento olímpico de sus consagraciones hacia el ideal del saber y de la consagración universal.

La humanidad en su ruta de investigación, impregnada su conciencia en el espíritu de la escolástica, preocupada en las concepciones trascendentales de la vida con prejuicios extracientíficos, explicaba los fenómenos naturales por la intervención inmediata y directa de la voluntad divina, anulando la crítica de la razón humana; y esa preocupación de la mentalidad sin la corroboración del espíritu de la naturaleza, fué llevada a la solución de los problemas de la criminalidad y de la delincuencia sancionando preceptos y principios de reprensión según fórmulas en los principios inmanentes y trascendentes de la razón filosófica, teológica y metafísica que se desprenden de la consideración del racionalismo de la época.

Se estudió el acto delictuoso en sí, haciendo abstracción del factor intrínseco de la personalidad, del agente del delito, de su conformación antropológica y de sus expre-

siones psicológicas del medio ambiente en que infinitas veces es la incubadora en la que se desenvuelven las modalidades específicas de las idiosincrasias delictuosas en la expresión de la actividad individual y social.

El desenvolvimiento de los estudios biológicos, la concepción científica de las modalidades de la vida, en la que las expresiones de la actividad mental responden al mecanismo del conjunto psico-biológico, a la estructura cerebral como palanca de la ideación, de la voluntad, de la cerebración consciente, y de las facultades afectivas, encaminaron el problema de la delincuencia a estudiar el agente según la conformación y estructura psico-antropológica como base del criterio de la imputabilidad.

El fenómeno del conjunto, como determinante de la acción impuesta por la compleja estructura del hombre, fué haciendo cada vez más difícil la solución analítica de los factores eficientes del fenómeno y dando al estudio del problema la puntualización de una complexidad máxima.

Se desprende de esas consideraciones que el acto delictuoso emana de múltiples determinantes de causas, cuyo estudio debe preocupar la mentalidad de la ciencia contemporánea.

La vida física de la raza, la salud corpórea, la estática y la dinámica del organismo humano como fundamento elemental de todo acto volitivo y de toda manifestación sensitiva como expresión del yo como individualidad pensante y expresión afectiva con todo el conjunto de modalidades psicológicas que emanan de ese postulado, el estudio del medio social étnico como climatérico, etc., la herencia espiritual de la tradición y de la historia, siguiendo el recorrido parabólico que toca a la civilización recorrer para el afianzamiento de sus grandes destinos.

Basado en los delineamientos fundamentales de esas concepciones científicas en lo que respecta a la represión racional de la delincuencia y del crimen en las naciones americanas.

El que abajo suscribe, presenta a la consideración del Segundo Congreso Científico Panamericano a reunirse en Wáshington en diciembre de 1915, las siguientes proposiciones indicadas para la represión científica y racional de la delincuencia y del crimen en las naciones americanas.

1. El Segundo Congreso Científico Panamericano, reunido en Wáshington en diciembre de 1915, vota las siguientes proposiciones indicadas para la represión científica y racional de la delincuencia y del crimen en las naciones americanas:

1°. El Segundo Congreso Científico Panamericano, reunido en Wáshington en diciembre de 1915, patrocina la creación en las naciones americanas de dispensarios para los niños nerviosos en donde se darán cuidados apropiados a los jóvenes epilépticos, histéricos y neurasténicos, a los niños tristes, perezosos, a fin de vigorizar la vitalidad, la nutrición de su cerebro y su cohesión mental.

2°. El Segundo Congreso Científico Panamericano, reunido en Wáshington en diciembre de 1915, patrocina en las naciones americanas el cultivo y el desarrollo intensivo de la instrucción y de la educación, impregnando el espíritu del niño en los principios luminosos de las verdades y de la moral.

3°. El Segundo Congreso Científico Panamericano, reunido en Wáshington en diciembre de 1915, patrocina en las naciones americanas la investigación médico-legal e investigación psicológica del inculpado, como procedimiento de ley.

4°. El Segundo Congreso Científico Panamericano, reunido en Wáshington en diciembre de 1915, patrocina en las naciones americanas la creación de hospitales-cárceles para los criminales alienados o grandes neuróPatas.

5°. El Segundo Congreso Científico Panamericano, reunido en Wáshington en diciembre de 1915, patrocina en las naciones americanas la creación de colonias penales, en donde se redimiría el criminal por el trabajo y los sanos ejemplos.

6°. El Segundo Congreso Científico Panamericano, reunido en Wáshington en diciembre de 1915, patrocina en las naciones americanas la intensificación de la lucha contra el alcoholismo.

7°. El Segundo Congreso Científico Panamericano, reunido en Wáshington en diciembre de 1915, patrocina en las naciones americanas la intensificación de la lucha contra las enfermedades infecciosas.

8°. El Segundo Congreso Científico Panamericano, reunido en Wáshington en diciembre de 1915, patrocina en las naciones americanas la reforma de la legislación penal, adaptada a los estudios psico-antropológicos y sociales contemporáneos.

Defensa profiláctica del niño contra las enfermedades infecciosas. Creación de un Instituto Inter-Americano de Profilaxia infantil de las enfermedades infecciosas:

El niño está expuesto por la vitalidad menor de su resistencia orgánica a los embates de todos los factores que pugnan con la estabilidad fisiológica de su ser; está colocado en uno de los eslabones de la cadena evolutiva de la vida al pasar por todas sus fases de la existencia. Su organismo sufre las reacciones psico-orgánicas más intensas, desde que los procesos del intercambio orgánico están en el período del acrecentamiento más progresivo, cualquier factor que venga a interrumpir la marcha evolutiva del complicado engranaje de sus intercambios orgánicos y de sus manifestaciones psíquicas se traducirán con caracteres indelebles en los procesos ulteriores de su ser en las características de una complexidad patológica y enfermiza. La salud del niño reposa sobre la perfecta armonía de los deberes cumplidos y los derechos adquiridos que la sociedad le dispensa, y cuán grande es ese deber desde que en estado latente la civilización humana, lleva en su energética y dinámica el factor intrínseco de la modalidad infantil de una antigua generación descentralizada en la evolución de los seres en el consorcio colectivo. Podría decir si se me fuera dable expresarme en una terminología metafórica que los microbios patógenos tienen en la infancia el perfecto caldo de cultivo, que necesitan como inoculación y reproducción desde que en ella la vida tiene los encantos de una oxigenación continua y perenne; y que los agentes patógenos se adaptan para su vivificación a detrimento de la salud individual y social. Trascendental es la solución del complicado fenómeno de la profilaxia de las enfermedades infecciosas de la infancia, es un problema de todos los órdenes de la actividad, si bien de puntualización médica, el conjunto de los factores que entran a dirigir la sociedad le deben no obstante, la dedicación más consagrada como previsión y terapia de esas manifestaciones de la patología pediátrica.

La medicina ha comprobado, corroborado infinitas veces, la precaria situación higiénica en que se halla el niño en la sociedad para resistir a los embates del contagio y la enfermedad.

En las primeras etapas de la civilización, cuando se desconocían las múltiples manifestaciones del contagio y de la evolución de las enfermedades, el problema en cuestión permanecía cual incógnito en la penumbra metafísica y trascendental; posteriormente el desarrollo del estudio de las ciencias naturales y de la biología, vino a despejar en parte esa obscuridad y en la clarovidencia de la ciencia de la experimentación, la gran palabra, el gran aserto de la microbiología a cuyo término el genio de Pasteur se destacara fulgurante en el escenario de la ciencia se conformó el determinismo de causa y efecto en las enfermedades infecciosas.

El problema en cuestión sufrió entonces una gran faz en su evolución, la ciencia triunfó sobre la antigua filosofía de lo trascendental y lo inmanente. Las autoridades sanitarias de las naciones civilizadas del orbe abrieron un gran capítulo a su estudio y la acción oficial dejó sentir su influencia bajo la aseveración de la palabra científica.

No obstante la solución del problema se esbozó más complicado que en la enunciación de sus principios, algunos resortes del engranaje complicado de la dinámica infantil pasaron desapercibidos, y esos factores descentralizados de la consideración científica explicaron la deficiencia de algunos puntos en la solución del problema sanitario.

Como dijera anteriormente, el problema debió solucionarse en los múltiples factores convergentes y que crean el campo en el que se desenvuelven las aptitudes vitales de la infancia.

La situación económica de la familia es uno de los puntos de capital importancia, para el juicio general que sobre las enfermedades infecciosas explican muchas veces la accidentada situación higiénica de la familia y del inmediato peligro para la vida de los pequeños seres evolucionando dentro de un medio en el que las exi-

gencias inmediatas de la nutrición orgánica se hacen con la deficiencia de la carencia de los recursos indispensables para la satisfacción florida de las necesidades materiales de la vida.

Sería el punto en cuestión el factor económico de la miseria, uno de los que predisponen al contagio de las enfermedades infecciosas, desde que ese niño sobre quien pesa esa situación aflictiva del hogar, no concentra las modalidades de resistencia orgánica propia de los atributos de las asimilaciones nutritivas de los intercambios vitales de la existencia.

A la consideración del factor económico debemos definir otra cuestión.

La mentalidad, el estado de cultura de las familias, el desconocimiento de las nociones más elementales de la higiene individual y colectiva, hacen y determinan en las familias así afectadas ese rasgo de deficiencia. El fundamento esencial sobre el que reposa la vitalidad del ser en los primeros años de la existencia es la higienización de los medios en que se desenvuelven los factores de la vida.

Estas dos deducciones las he podido corroborar en mi práctica profesional, en donde en cierta y determinada vivienda de algunos barrios apartados de la capital, la pobreza más grande impera y la deficiencia más grande de los medios higiénicos crean y predisponen a las infecciones patógenas más mortíferas.

He podido comprobar en las epidemias que anualmente atacan la población, una dejadez marcada de los preceptos de la higiene.

La lucha por la profilaxia de las enfermedades infecciosas en la infancia debe llamar en consideración la intervención de los Estados en una sabia disposición actuando en el sentido más amplio del saneamiento de la población.

El problema en cuestión exige legal y moralmente la constitución de un Instituto Inter-Americano de Profilaxia de las enfermedades infecciosas de la infancia:

1°. El Segundo Congreso Científico Panamericano, reunido en Wáshington en diciembre de 1915, patrocina la creación de un Instituto Inter-Americano de Profilaxia de las enfermedades infecciosas de la infancia.

2°. El Instituto Inter-Americano de Profilaxia de las enfermedades infecciosas de la infancia, hará práctico el cumplimiento de los preceptos higiénicos y de la profilaxia de las enfermedades infecciosas por una reglamentación legal de los Estados americanos.

3°. Por conferencias públicas llamadas a ilustrar a los pueblos americanos el sentido de una defensa racional y científica contra el virus patógeno.

4°. Por la publicación de folletos explicativos fáciles de comprensión popular y con fotograbados enunciativos de las causas y patogenia de las enfermedades infecciosas en la infancia y el modo de evitarlas.

5°. El Instituto Inter-Americano de Profilaxia de las enfermedades infecciosas de la infancia, encomendará a una comisión científica de cada nación americana la cooperación efectiva de los fines y móviles del mismo.

The CHAIRMAN. The symposium on cancer will be opened by a paper by Dr. Leo Loeb on "General tendencies and problems." I take pleasure in presenting Dr. Loeb.

GENERAL PROBLEMS AND TENDENCIES IN CANCER RESEARCH.

By LEO LOEB,
Washington University Medical School.

After the successful continuous transplantation of rat sarcoma and mouse carcinoma had shown that we possessed a method suitable for the study of the biology of tumors, and promising a rich harvest of results, the decade following the year 1901 was to a great extent devoted to the study of propagated tumors rather than to the analysis of the first origin of tumors, although this latter problem had never been entirely neglected. Within recent years, however, much attention has been given to the first origin of tumors. The so-called endemic occurrence of cancer which we observed in the case

of cattle and rats, and which other investigators observed in the case of mice and other animals, suggested to us 16 years ago the possible significance of heredity as an etiological factor, Some years later, observations which we made in a mouse-breeding establishment in Granby confirmed this hypothesis; but it is only during the last six years, following the observations of Tyzzer and Murray, that our investigations in conjunction with Miss Lathrop proved on a very broad basis the very great significance of heredity in the transmission of cancer in mice, the distinctness of the age and frequency factors, the correlation between cancer frequency and structural and functional characteristics of the animals. The results of hybridization experiments, which we carried out on a large scale, do not seem to be compatible with the view recently expressed that the tendency to cancer is a recessive character.

These studies and the methods used therein have, however, a much wider significance. On the basis of a thorough knowledge of the cancer incidence in certain families, and on this basis alone, will it be possible to analyze certain other factors in the etiology of tumors, and the understanding of these latter factors, as well as of heredity, will perhaps ultimately provide us with a rational basis for the prevention of cancer. Without a thorough knowledge of heredity, conclusive results as to the significance of other factors could not be expected. Acting on this principle, we found that castration in sexually mature mice at the age of 3 to 6 months reduces the cancer rate in a very pronounced way.

Prevention of pregnancy, while it still has some effect in reducing the cancer rate, has very much less significance than castration. These results, and some additional ones to be mentioned shortly, permit us to classify the causes of tumors into two main divisions—internal and external ones. Heredity belongs to the former class. The point of attack of these hereditary factors we do not yet know. In some cases they may perhaps stand in relation to some other internal factors, which are in all probability of significance in certain cases. I refer to the spontaneous parthenogenetic development of the egg within the ovary and perhaps elsewhere in mammals—a process which, according to our findings in the guinea pig, is not a rare occurrence, and may even normally proceed to the formation of the anlage of the central nervous system. To this class of factors may also belong developmental errors which were already suspected by Cohnheim, and which, as we know, may appear as inheritable mutations in various groups of animals.

The external factors may be further divided into chemical and mechanical, and both may be derived either from within the body or from the outside world. As an example of a chemical factor originating within the body we may cite the great importance of the internal secretion of the corpus luteum in the origin of cancer in mice, to which we referred above, but other internal secretions will probably be found to be of similar significance. External mechanical factors can be recognized in the well-known effect of chronic irritation. How far certain parasites, especially those in the class of vermes and insects, produce cancer through chemical and how far through mechanical means is not certain. Previous observations in man in the case of cancer of the bladder caused, directly or indirectly, by bilharzia, and especially the recent experiments of Fibiger, make it, however, quite certain that such parasites may be the cause of cancer. It is likewise uncertain how far Roentgen ray cancer, frequent in Roentgen ray operators, and also apparently experimentally produced in a few rats by Marie, is due to ulceration subsequent to the exposure or to a direct stimulating action of the rays. In some cases perhaps chemical and mechanical factors may cooperate in producing tumors; the efficiency of such a combination in calling forth tumorlike formations has been shown by us in the case of deciduamata of the uterus, which we produced experimentally—a new formation which we included in a class designated as transitory tumors.

There are observations on hand which indicate that growth stimuli may be especially active in animals with a hereditarily determined tendency to cancer. Such an

observation we made in the case of a cancer in a mouse belonging to a family rich in tumors, where ulceration of the skin near an adenoma of the mammary gland led to the development of an epidermal carcinoma. Further systematically conducted experiments in this direction might lead to interesting results.

It is, however, not probable that in order to obtain the production of cancer the quantity of prerequisite internal factors must be a definite one. On the contrary, there is some evidence on hand which makes it probable that internal and external factors may vary in inverse ratio, and that if the external factors are quantitatively very strong, the quantity of internal factors may be reduced.

If we survey briefly the various types of growth reactions known in vertebrates, we may perhaps, according to the character of the stimuli, which are usually in each case the first members in a complicated reaction chain, and of the systems on which they act, provisionally distinguish the following types:

1. Various stimuli act for a short time on complex systems, the egg cells, and lead to a long chain of growth phenomena, which ultimately cease. The experiments in artificial parthenogenesis of Jacques Loeb led to a very far-going analysis of these phenomena.

2. Defects lead to a chain of growth phenomena which are of a temporary character, and come to a standstill after a certain quantity and kind of new-formed tissue has more or less completely filled out the defect.

3. Chemical substances stimulate the growth of certain tissues to which they bear a more or less specific relation.

These growth phenomena come to a standstill with the activity of the stimulating substance or very soon afterwards. (Corpus luteum and mammary gland.)

4. A combination of factors 2 and 3 may lead to tumor-like growth phenomena when either factor alone would cause only a slight proliferation. Here, again, the effect is temporary. (Experimental deciduomata of the uterus.)

5. Chemical (lipolytic?) bodies which do not show a specific relation to the organs affected stimulate various tissues to a temporary proliferation: Fat soluble stains (Bernhard Fischer and others), ether (Reinke), are substances that under certain conditions seem to exert a stimulating effect.

6. Chemical and mechanical factors produce with the aid of a large quantity of internal factors, or in certain cases apparently without such aid, an increase in cell proliferation that persists after the stinuli have ceased, which is permanent, potentially eternal, in contradistinction to the temporary reactions mentioned above. This is the cancerous reaction with which all or the large majority of the mammalian tissues may respond. Characteristic for this reaction is neither potential immortality, (some, or perhaps all, somatic cells are potentially immortal), nor the power of continued proliferation which in all probability even certain ordinary somatic cells possess; but it is the increase in proliferative power which is characteristic of cancer, and furthermore the permanency of the reaction in response to a temporary, nonpermanent stimulus. We have, then, to assume that a labile cell system which responds to temporary stimuli with a temporary reaction is transformed under the influence of certain stimuli and often with the aid of hereditaty factors into a stable system which shows a greater proliferative power than the labile system. The stimulus brought thus about merely a transformation of the cells into a new kind of cell system, which proliferates indefinitely at a more or less increased rate. Such a transformation may be called a mutation. Inasmuch as all or the large majority of all body cells are liable to this change, they must have from the beginning in their organization a mechanism that provides for the possibility of such a mutation.

According to this conception we must then assume that all or most cells have potentially two equilibria—the normal one and the cancerous. They begin life with the normal equilibrium, but under the influence of certain stimuli, with or without the cooperation of hereditary factors, they are transferred to the cancerous equilibrium.

Cells in the normal equilibrium react to stimuli in the manner indicated above (types 1 to 5). Ultimately they return invariably to the normal equilibrium after the stimulus has ceased to act: Cancerous cells, on the other hand, may perhaps be exterminated, but they are not known to return to the normal equilibrium. There is, however, an alternative to this conception which would eliminate the necessity for assuming a new equilibrium for cancerous proliferation—an assumption for which naturally no anology can exist. If we assume that an external agent associated with the cell rather than a physical-chemical mechanism within the cell produces the cancerous proliferation, the latter would no longer represent a peculiar unique condition, but would be a special application of one of the types 3 to 5, in which, however, the stimulus would act incessantly. Such a stimulus could be supplied through multiplying microorganisms which essentially represent constantly newly formed external chemical stimuli. We know that microorganisms can call forth cell multiplication in plants and animals. In plants certain bacteria can produce, as especially Erwin Smith has shown in the case of the crowngall, tumor-like proliferations—an effect in this case not depending merely on the kind of stimulus, but also on the particular system on which the stimulus acts.

In this connection we might also mention a number of extremely interesting cases in which various investigators saw the transformation of different normal into cancerous tissues, after a preceding contact with cancerous tissue of another kind, but in tissues of the same individual. I referred above to an observation of this character in which we found skin to become cancerous under the influence of an adenocarcinoma of the mammary gland. Similarly, in contact with carcinoma, connective tissues may become sarcomatous. Such tumors we called combination contact tumors. In such a carcinosarcoma in a Japanese mouse which we studied experimentally we found the carcinomatous and sarcomatous components to follow the same variation curve of growth energy in succeeding generations. This suggests the identity of the agent causing the proliferation of both tissues and the dependence of the variation in growth on the variation in the activity of the agent. The agent transferred from one tissue to another might be a chemical substance—an explanation first suggested in the case of the sarcomatous transformation of the stroma by Ehrlich and Apolant—or it might be a microorganism. There exist already normally indications pointing to a chemical influence exerted by one tissue upon another. We interpreted in this manner the difference in cell activity in the connective tissue of the mucosa in certain organs near the epithelium on the one and near the submucosa on the other hand. The different effect exerted by the tissues of different individuals on the activity of the fibroblasts of the host also points to such a conclusion (different effects of auto and homoiotransplantation).

There are especially to be considered the very important results of Peyton Rous, who succeeded in fowls with means which in the case of mammalian tumors had not led to positive results in the hands of earlier investigators, to separate through filtration and other means the causative agent from the sarcoma cells with which it was associated. In this case we might have to deal either with filterable microorganisms or again with chemical substances. If we accept the latter alternative, we would have to assume that the same substance that initiates the cancerous cell proliferation in normal cells would, after the change has once been accomplished, be perpetually newly formed within in the proliferating cells. This condition would in some respects be comparable to an autokatalytic process. The cancerous equilibrium would represent a condition in which this growth substance is either produced in a larger quantity than it exists in normal cells, or is entirely formed de novo. It seems, furthermore, that no antibody is produced in the body fluid against this substance. These substances do not seem to be separable from the cells in all fowl tumors, and the kind of fowl tumors in which a separation can not be accomplished behave in this respect like the mammalian tumors. There seem to exist different substances of

this kind, and different substances always call forth a specific activity of connective tissue cells resulting in the reproduction of the original kind of tumor and stimulating endlessly the production of the same specific substance within the fibroblasts. Just as in the case of the corpus luteum substance responsible for the production of deciduomata, the cooperation of a mechanical factor seems to be essential for the stimulation of tumor growth in fowl. Thus we would have most probably to interpret these phenomena if the observation of Casimir Funk, according to which an alcoholic extract of the tumor contains the active agent, could be confirmed in a larger number of cases. If this should prove correct, we may expect to find corresponding conditions in mammalian cancer. A study of heredity in cancer of the fowl would close this chain of investigations, and we could then, with the analysis of internal and external factors in cancer already on a solid foundation, conclude that the causes of cancer have in their main outlines been satisfactorily analyzed. Of course underneath this first plane of causes connections extend further into fields where they meet with other factors determining cell and tissue life in its dependence on physical and chemical laws, and thus we are led into deeper planes of causation. But here the problems have become identical with those of general biology.

In this connection a few words concerning the definition of cancer might not be out of place. It might be assumed a definition of cancer satisfying past and future research to be one of the essential requirements for the fruitful conduct of investigation on the contrary, I believe that at the present stage of investigation progress may be retarded through premature rigidity in definition, and especially through insisting on the proof that secondary tumors originate from transplanted cells. In the case of sarcoma of the rat and mouse this proof has so far been supplied only the rat sarcoma of the thyroid found in Chicago, and is merely based on analogy in the case of the large majority of other sarcomata. Since it has now been shown that in sarcoma of fowl and agent associated with the tumor, but separable from it, may just as well give origin to new growths, we may well hesitate in excluding from consideration new formations which under certain conditions take in all probability origin from transplanted cells, while in other cases they may perhaps be propagated through an agent associated with the tumor. I refer especially to the so-called lympho-sarcoma or small round cell sarcoma of dogs, which, after transplantation in dogs, apparently grows from the transplanted cells, while in the fox, according to von Dungern, the tumor cells are composed of host tissue. May we not, in case von Dungern's view should prove correct, have to consider the possibility that the transplanted dog cells perished in the foreign species and that the associated agent stimulated the host cells to proliferate?

With the factors which we have already analyzed—factors of heredity, of internal secretion, of external chemical and mechanical stimulation—we are in a position to control to a great extent the cancer rate in certain species of animals. As we said, we can not yet exclude with certainty the other alternative—namely, microorganisms—as an additional causative factor.

After so many futile attempts at a direct proof of their presence, further efforts of this kind do not appear promising at present. There seem, however, ways still open to approach this problem in an indirect manner.

To decide between the two alternatives which we mentioned does not only concern cancer research in the more restricted sense, but is of the greatest importance for general biology. In return for much that it received from neighboring sciences cancer research has given something important to biology. The serial endless experimental propagation of tumors has enriched biology with a valuable instrument of research and new outlooks on the life and character of somatic cells have been gained. We may briefly mention the following facts established or very strongly suggested: In the course of our early transplantations we found that the energy of tumor growth can be experimentally increased as well as decreased. Ehrlich explained the increase

as due to a selection of rapidly growing tumors. We, however, believed from the beginning that it was partly produced by a mechanical stimulation of the tumor cells and in addition was possibly due to chemical stimulation caused by the transfer in to a new host with a different constitution of the body fluids, in some cases perhaps processes of immunity may enter into this phenomenon.

In conjunction with M. S. Fleisher we noted that chemical bodies which inhibit tissue growth at a certain period in the life of tumors do not have this power at other periods; especially are they powerless in the case of very young tumors—an observation confirmed by Keysser; but we found that such early injections produce an immunization against the later action of these substances. Our experiments suggest, furthermore, very strongly that this immunity is of a twofold character; that it originates in the host as well as in the tumor cells themselves. That this cell immunity can be transferred to a certain number of later cell generations and is to some extent specific for the substance which had called it forth. While our results, based on the observation of a very large number of animals, strongly suggest these latter conclusions, we nevertheless think it desirable to add new evidence in order to guard against a complication with variable factors.

Do we have in all these cases to deal with indirect actions on the cells and with direct actions on accompanying microorganisms, or with direct actions on the cells? I rather incline to the latter view, and we would suggest that an increase in chemical activity in the tumor cells—an increase perhaps restricted to certain activities—render the latter a much finer balance in their response to certain environmental conditions through variations in growth energy than are the normal tissue cells.

As we pointed out in 1901, on the basis of Moran's and our own experiments, cancer cells are potentially immortal in the same sense in which protozoa and germ cells are potentially immortal. All, or at least the large majority of all, normal tissue cells are potentially cancer cells, and we may therefore, with full justification, conclude that ordinary somatic cells are likewise potentially immortal. Like the majority of tumors they can not be indefinitely propagated in other individuals of the same species because of the injurious action of what we may term "homoiotoxins." On the other hand, thanks to their increased growth, energy, and perhaps a lessened sensitiveness to homoiotoxins, the cells of certain tumors can overcome the injurious conditions existing in other individuals of the same species and be propagated indefinitely. Tumor cells and ordinary tissue cells do not differ, as Bashford and others assumed in potential immortality, but in the intensity with which they proliferate and in their destructive power.

Of equally great biological interest are the defensive reactions called forth in the host through the growth of the tumor cells. As one of the most important results, we may here state that no immunity seems to be produced through tumor growth in the animals in which the tumor originated. We found that in the case of rat and dog tumors cells remained alive and grew after transplantation into the animal in which they originated, while they died in other individuals of the same species. Tyzzer found the same to be true in the chicken, and Harland and Fleisher and ourselves in the mouse. Harland's experiments suggested, furthermore, that the own tumor could not act as antigen, and by proving, in addition, that the own tumor does not neutralize immune substances, our experiments prove the correctness of Harland's suggestion that against an autochthonous tumor no immunity can be produced. The greater significance again attached to the study of animals in which tumors originated, in contradistinction to bearers of experimental tumors, is one of the characteristic tendencies of recent cancer investigation, and it is of interest in this connection that our experiments indicate that animals with autochthonous tumors are a better soil than normal animals for the growth of other spontaneous tumors. While, therefore, in the own organism usually no reaction takes place against tumor cells, reactions take place after transplantation of tumor cells into other individuals. These reactions

are essentially of a similar character in the case of tumors and of normal tissues. Again, the correlation between the behavior of normal and of cancerous tissues has proven fruitful in this case. After autotransplantation of a piece of normal tissue it may, in the same way as a piece of tumor, at least in the case of certain tissues, apparently live indefinitely, while after homoiotransplantation, as we observed, the tissues die as a result of the attack by lymphocytes and through the influence of fibro blasts of the host, producing dense fibrous tissue, which strangulates the foreign cells.

There exists a possibility that the strange body fluids may also directly interfere with the metabolism of certain transplanted tissues to such an extent that they are severely injured. After heterotransplantation the indirect injurious action of the body fluids, which are unsuitable for the metabolism for the transplanted cells, is more pronounced and leads to the early death of the transplanted cells, and we found in the case of skin under these conditions no noticeable activity on the part of the lymphocytes and fibro blasts. J. B. Murphy showed, however, recently in very ingenious experiments that also in the case of heterotransplantation, lymphocytes may be of importance as a defensive mechanism of the host under certain conditions.

Likewise in the case of tumors against which an immunity becomes established lymphocytes play a distinct rôle in the destruction of the tumor tissue, as the investigations of Burgess, Baeslak, Da Fano, Rous, and J. B. Murphy have shown. This holds good in the case of tumors already established. If immunity is produced before the transplanted tumor has united with the host tissues, the ingrowth of fibro blasts and blood vessels into the transplanted tissue may, according to Russel (in the case of tumors) and Peyton Rous (in the case of embryonic tissues) be delayed or else diminished in amount.

As the most probable explanation for these phenomena we proposed the following theory: The chemical incompatibility between the body fluids of one individual and the tissues of another lead to changes in the metabolism of the tissues, with the production of homoiotoxins and heterotoxins, which, if they do not exceed a certain strength, disturb to some extent the normal functions of the transplanted tissues, without, however, interfering seriously with their life; but the abnormal products formed attract the lymphocytes and alter the reaction of the fibro blasts, which latter are induced to produce dense fibrous tissue. If the poisons become more active, they may directly injure tissues to such an extent that growth and life become impossible.

These conclusions, as we believe, also throw light on so-called chronic inflammatory processes of various organs where a changed metabolism of the cells and may be also poisons produced by microorganisms may induce fibro blasts to form bands and attract lymphocytes, thus leading to processes of cirrhosis. In a similar way, in the case of tumor immunity, which exists, for instance, in the case of the retrogression of tumors, as Clowes and Gaylord have shown, substances produced as a result of the immunization and circulating in the body fluids alter the metabolism of the tumor cells, which now likewise influence the activity of the lymphocytes and fibro blasts in a similar way as normal tissues in a strange host.

It remains for further investigations to decide how much the presence of foreign tissues leads to the direct production of what we could call primary homoio and heterotoxins, and how much it leads as the result of immune reactions to the production, secondary homoio and heterotoxins, the immune substances. At present it appears probable that both these substances play a rôle. Apparently in vitro the toxicity of body fluids of foreign species is less marked than is vivo. We must, however, consider that the amount of body fluids and of toxin acting on the tissues in vitro is extremely small as compared with the quantity acting in the living body. In the case of both types of substances those preformed and those produced through immunization, we are able to point to the existence of analogous substances existing elsewhere—namely, the preformed species specific tissue coagulins and the secondarily, arti-

ficially produced antibodies of various kinds. It also remains further to be determined how far the metabolic products of foreign cells exert a direct influence upon each other and how much of this effect is dependent upon the interaction between cells and foreign body fluids.

In addition to the effect of toxic substances, mere lack of common foodstuffs can also retard tumor growth, as the retarded growth of transplanted tumors in pregnancy and the feeding experiments of Moreschi, Peyton Rous, Beebe, Sweet, Corsen White, Saxon, Robertson, and Burnett have shown. Whether an immunity caused through the lack of specific substances in contradistinction to the common food and growth stuffs of cells, whether an athreptic immunity, as Ehrlich called it, exists, is however very doubtful. Such an athreptic immunity certainly would not explain the phenomena referred to above.

In connection with the studies in metabolism to which we have just referred, we may look forward to interesting results through further analysis of the chemical constitution of tumor tissue.

I am, however, inclined to regard differences so far found between normal and tumor cells in a similar light, as differences observed in the case of the mitotic division in normal and tumor cells, both being probably the result and not the cause of the changes in the growth energy characteristic of tumor cells.

Having arrived at the end of our survey we must confess that much remains still to be done before these investigations can in anyway be considered near completion.

On the other hand, I believe to have indicated that there are ways still open for further attack of the problems of cancer and tissue growth, and I hope also to have been able to convey the impression that the work of so many investigators in this field has not been in vain, and that not only this special branch of science has been built up, but that also biology and pathology in general have been stimulated and enriched as the result of their labors.

The CHAIRMAN. We will continue the papers and discuss them en bloc at their conclusion. I have the pleasure of introducing Dr. Maud Slye, of the University of Chicago, who will read to us a paper on "Experimental studies in heredity."

EXPERIMENTAL STUDIES IN HEREDITY.

By MAUD SLYE.

University of Chicago.

I wish to give to-night a condensed report of my work of the last 10 years along two lines—the inheritability of tumor and a few points on its etiology. The material for this study has been in my hands for 10 years. During the first five years I was engaged in studies on general problems in heredity, in which the main line of attack was on the inheritability of coat color, the inheritability of coat pattern and the inheritability of what I may call general metabolic condition as manifested in size, shape, coat quality, pigment, reproductive capacity, and length of life. During these five years strains of mice were established which had resulted from these various lines of study and from this material as a basis I began the work on the inheritability of cancer. The stock therefore shows many things of great interest outside of its cancer potentiality—viz, the relation or nonrelation of cancer to these various factors that I have mentioned, coat color, general metabolic condition, etc.

There are many opportunities for error in the study of any problem in heredity, because individuals that are poorly housed or poorly fed never produce their full quota of young, and it is impossible to base any conclusions on one or two litters of

three or four mice each. It is necessary therefore for any conclusive study in heredity that a large percentage of the mice should live to old age, producing their full quota of young with a variety of mates, since the progeny of any hybrid individual will depend upon its mate and not alone upon itself; for example, a first-generation albino mouse, derived from red, if mated with a gray will produce red in the first generation. It is the mating here with the gray which determined the production of that red young, since if an albino had been mated with any other albino it never would have produced any other than whites.

Again, many of the mice are eaten or killed at birth. There is only guesswork to tell what they might have been. Again, it is impossible to base any conclusions on small numbers, since what happens for ten times may fail in the next ten. And still again, as I have already pointed out, a variety of mates is necessary to show from any given hybrid all the possible offspring.

Especially are these errors likely to obtain in the study of cancer, since this disease does not occur in early life and a mouse which dies before showing cancer must be classed as noncancerous, no matter what its potentialities may have been. It is only by breeding out the offspring of such mice that we can determine whether or not they carried tumor possibilities. The full potentialities of cancer, therefore, in any strain can never be fully known until every individual lives its full term with a full output of offspring.

This report to-night is based on 12,000 autopsies performed during the last six years, which include a thousand cases of tumor, involving over 2,000 malignant growths. The experiments at the present time are being carried on with a living stock of some 12,000 mice, which in its present state is producing a steady output of from 75 to 100 cancer patients all the time.

My tumor stock came from three original lines of wholly unrelated mice. The first was a strain of Japanese white-footed mice, a piebald gray-white, from which I have in process of making at the present time Japanese waltzing mice. Through the first five years of work it was hybridized with mice of all possible coat colors, thus giving these piebald mice of various pigments. It carried a heavy percentage of cancers through a great many of the different organs, and is represented in the charts by strain 90 (I will make this clearer in demonstrating the charts). The second stock of mice was an albino stock, very nearly depleted at the time the cancer work began. It carried tumors of the mammary gland and of the lung and did not produce any tumors in other organs. The third stock was secured from the Granby, Mass., breeding establishment. This stock included albinos, red, black, blue, gray, chocolate, and practically every color of mice known to modern work of this type. Throughout the entire stock it carried very little outside of mammary gland and lung tumors.

In demonstrating the charts, which I have to do very hurriedly indeed, there are two things to be shown. First, the general fact of the transmission of cancer; second, the transmission of types and locations of cancer; for these stocks of mice and their hybrid offspring have been so far manipulated at the present time in breeding that they will produce practically any type of tumor desired.

Strain 139 was some of the Granby, Mass., albino stock, inbred for 23 generations; 6 generations in my hands. This chart represents all that was left of it when my work in cancer began. Every mouse in the family at that time that lived to cancer age, with the exception of male No. 553, showed tumor at death, nearly all of them tumor of the lung. This mouse (male No. 553) died of pulmonary infection when he was barely 6 months old. Throughout all the study of cancer in my laboratory we have found, and particularly in these lung tumors, all stages of a chronic condition frequently eventuating in tumor. This mouse showed a chronic condition very common in the lungs of mice which later develop lung tumor. It is a fair inference that he would have developed tumor of the lungs, but at any rate the strain shows 90 per cent of tumor; wherever it was hybridized it produced a very high percentage of tumor.

I have a strain now (strain 65) carried out in two branches. If you glance through it, you will note that the parent female came from strain 139, the parent male from strain 90, the strain of the Japanese piebald mice that I spoke of. This is an extracted gray-white piebald strain. In respect to coat color and coat pattern it follows the male; in respect to tumor tendencies it follows the female, since this strain throughout all the time that I have handled it has never shown anything but mammary gland and lung tumors. I could reproduce that type of chart very extensively, but I have not brought these with me because I wished to show to-night this later work on the transmission of liver tumors.

In the literature there have been few reported liver tumors, either in mice or in the human species; or, for the matter of that, in any other animal species. This strain 90 carried a heavy percentage of liver tumors, and I wish to show you some of the results of hybridization of that strain. Let us start with this large chart, which shows you how these strains are derived. The main emphasis to-night I wish to place on strain 338, which you will see on the other side of the room. It has been bred out in a great many other branches beside these shown here. This chart shows the history of strain 338. Going back three generations, the female was derived from strain 138, Granby, Mass., red stock. This red strain did not breed true in color. It carried only cancers of the mammary gland and of the lung, and it never showed any sarcoma; it showed only carcinoma. This parent female was mated with a male from strain 90, which was that Japanese white-footed strain which carried both sarcoma and carcinoma involving tumors of the mammary gland, lung, testicle, kidney, mediastinum, and lymph glands. The resulting strain from this cross (strain 21) carried both sarcoma and carcinoma; these tumors being located in the mammary gland, lung, liver, testicle, and jaw. This female of strain 21 was mated with a male from strain 135. The latter strain came from crossing strain 151 again with strain 90. The resulting strain, strain 135, showed only mammary gland and lung tumors. In its ancestry, however, was strain 90 carrying tumors of the mammary gland, lung, liver, testicle, ovary, mediastinum, and lymph gland. A double dose of this combination, then, was bred in, since it ran in both the male and female ancestry.

From this cross the resulting strain in the maternal ancestry was strain 112, which carried cancers, both carcinoma and sarcoma of the mammary gland, lung, liver, kidney, face, pelvis, and leg, practically duplicating the list with one or two exceptions and one or two additions. On the male side, going three generations back, strain 94, the old albino strain that I spoke of, some of the original stock, carried carcinoma and leukemia. The tumors were located only in the mammary gland and lung. The mating here was with a male of the same stock, carrying in again the same thing. The female, then, two generations back was from inbred stock. The same thing is true on the paternal side of this branch of the family, where strain 90 came in in a double dose, giving an inbred member of strain 90 as the ancestor.

The mating of this male of strain 90 inbred, with this female of strain 94 inbred, produced strain 124, which carried carcinoma and sarcoma; of the mammary gland, lung, liver, and jaw. The mating of this male from strain 124 with the female from strain 112 produced this strain 338, which I wish to demonstrate more in detail. It carried leukemia and showed carcinoma, sarcoma and lymphoma; involving tumors of the mammary gland, liver, lung, back, jaw, chest, ribs, testicle, body wall, lymph glands, mediastinum, pelvis, hand, and preputial gland. From these matings which I have detailed, there is produced a strain which is absolutely riddled with cancer, in which there is scarcely an organ which does not carry tumor. I may say, in passing, that this strain carries a great many tumors into any strain with which it is hybridized. Strain 338 was started by the individual male represented over here in strain 124, Branch 1. You will notice here that the parent female of strain 124 carried adenoma of the mammary gland and adenoma of the liver in connection with liver cyst. There do not appear in this chart any further liver tumors, but the tumors are represented in the

lung only in this part of the family. Strain 124, Branch 2; here neither the female nor the male developed tumor. They nevertheless transmitted it in the first generation in a percentage which is rather striking, for this represents all of their progeny which lived to cancer age. The mating here of selected males and females in two different branches gives us in both cases the perpetuation of cancer. In this strain the male that I wished to emphasize—viz, this male No. 7736, died when he was 3 years and 3 months old with a beginning papilloma of the lung and arterio-sclerosis. If the mouse had died at any time within a reasonable age—any of you who know about the breeding of mice recognize that this is quite an exalted age—if he had died at any previous time, he would have been called strictly nontumorous. This male was the parent of strain 338.

The female which headed this strain 338, the individual female, is shown in strain 112 of which she was a member. This is the female No. 5417 which heads strain 338. She belongs in the third generation in strain 112 and had two carcinomas of the mammary gland and a carcinoma of the pelvis (which is not put down here), with metastases in the lungs. Her grandmother had an adenoma of the liver, and her grandfather a beginning lung nodule, like those frequently observed in connection with lung cancer. Here is a sarcoma of the liver, and here a carcinoma of the lung, here three carcinomas of the mammary gland with metastasis in the lung, and a squamous-celled carcinoma of the neck.

Now, bearing in mind how rare liver tumors are, for I am laying the emphasis to-night, from brevity of time, upon tumors of that particular organ—remembering how rare they are—will you please look over these charts. This parent female did not express tumor of the liver, but she came from a family with many cases of it and whose ancestral strain and its later derivatives carried liver tumor. The male, as I showed you over there, did not express tumor of the liver, but he came from a family which carried in its ancestry a high percentage of tumor of the liver. There went into the strain, strain 338, then, from both sides of the family a heavy percentage of liver tumor in addition to the other tumors bred in at the same time.

Branch 1; this is the parent female No. 5417. The parent male No. 7736 here. This is the parent generation which heads all these branches of strain 338. The female had two carcinomas of the mammary gland, and a carcinoma of the pelvis of an entirely different type from either of the mammary gland cancers; the male had a papilloma of the lung and he was this old male 3 years and 3 months old. The daughter of that mating had two carcinomas of the mammary gland and an adenoma of the liver. This is the female selected for the mating in this branch. In the next generation there is a sarcoma of the body wall and the lymph glands and a papilloma of the lung, almost a replica of the grandfather's papilloma. And in the next generation, again, two carcinomas of the mammary gland here, a carcinoma of the lung with lung metastases, and again three carcinomas of the mammary gland.

Branch 2 is not represented. Branch 3 shows here one of these beginning lung nodules. In the next generation a sarcoma of the back and further down carcinoma of the lung and of the mammary gland.

Branch 5 is one of the interesting charts, from the point of view of the liver tumors. Here again are these same parents female No. 5417 and male No. 7736, and here for the parents in this mating there were selected a female with two carcinomas of the mammary gland and a male with adenoma of the liver. I may say,what I omitted to say before, that all the offspring of female No. 5417 represented in these charts were produced after the appearance of her tumor. There are none of her young here represented who were produced before the appearance of her tumor. The mating of this female with two carcinomas of the mammary gland and this male with adenoma of the liver gives a family in which cancer is widespread; a male with carcinoma of the lung, a female with two carcinomas of the mammary gland, a squamous carcinoma of the face and abscess of the jaw (which looked

more like an entirely necrotic tumor but which was diagnosed as abscess), two carcinomas of the mammary gland, a carcinoma of the pelvis, metastases in the lungs, etc. Here were two carcinomas of the mammary gland. From the individuals selected for breeding in the next generation of those who lived to cancer age two showed carcinoma. Of those selected for breeding here, among their seven offspring there were four cases of carcinoma; in the fourth generation two cases of carcinoma of the mammary gland out of three (we have had to date) that have lived to cancer age. There were, as I recall it, seven cases of liver tumor in this one branch of the strain.

In Branch 7, from these same parents; there are no tumors in the first generation male or female chosen for the mating, but as I have emphasized repeatedly it is only by breeding these out that you can tell what their cancer potentialities are, since they are not necessarily expressed and since many of these mice die before six months, which has been taken as the lower limit of cancer age. But in the second generation here, out of five which have died to date, having lived to tumor age, there were three cases of carcinoma; and in the next generation out of six offspring there were three cases of carcinoma.

In Branch 11 we see how multiple tumors persisted in this branch. This female had two carcinomas of the mammary gland. There are two carcinomas of the pelvis in the next generation—a female with four carcinomas of the mammary gland and metastases in the lung. In the next generation, out of five who lived to cancer age four had cancer. One has developed an adenoma of the liver. In the next generation, in both the matings carcinoma of the mammary gland, and in this case there is again carcinoma of the pelvis.

In Branch 12 of this same strain, in the first hybrid generation, there are several cases of cancer. In the next chart, the parents selected for the mating did not show cancer; but in the next generation cancer came out in startling manner. Here a carcinoma of the mammary gland, with metastases in the lung, again two carcinomas, a testicle tumor, a malignant tumor of the preputial gland, and again a carcinoma of the mammary gland.

In the next generation here is a carcinoma of the mammary gland with metastases in the lung, and here an adenoma of the liver and an adenoma of the lung; and wherever that strain has been crossed in it has carried not only cancer but it has carried these specific types of cancer. In the mice who are dying now in those hybrid strains that have lived to cancer age I am getting almost a duplicate of these things which appeared sometimes many generations before them.

There are other charts here that show this predominance of liver tumors wherever strain 90 went in. Thus, as you see, the parent female from strain 90 and the parent male from albino strain 94, both of them tumor strains; here the carcinoma of the mammary gland, metastases in the lung, here carcinoma with multiple metastases in the liver, etc., besides the various other tumors.

I have one or two other interesting charts. Strain 196, on the maternal side, came from strain 90, and the parent male came from strain 94. The percentage here of tumor is extremely high, and this seems to be a branch of the family which got most of the ovarian tumors, for out of the entire 2,000 tumors in my stock only 14 are ovarian tumors. Of these 14 all but 4 were in this strain and its hybrids and allied strains. The other 4 were scattered. You will notice the predominance of ovarian tumors in this one. There bilateral malignant tumor of the ovaries, here carcinoma of the mammary gland, general sarcomatosis of nearly the entire system, bilateral endothelioma of the ovaries, squamous carcinoma of the skin, and carcinomatous cyst in the ovary which was just beginning to proliferate in a papillomatous fashion, here bilateral ovarian carcinoma, and down there a carcinoma of the left ovary.

Strain 104, which was a strain of wild mice, Peromyscus Californicus, local in the Santa Clara Valley, the stock had been in my hands some six years. Carcinoma and sarcoma are both rather rare in wild mice, at least rarely reported. Female 2999

had a squamous carcinoma of the jaw. She had a son with what was diagnosed as an abscess of the jaw, because no tumor cells were left, but it had every appearance of a necrotic tumor. The mating of these two produced a third with squamous carcinoma of the jaw. That is rather interesting as showing the transmission of the type of tumor within a strain, since in all the Peromyscus stock that I have had in my laboratory in 10 years there has never been another case of it.

In strain 164 we have a wild house mouse male mated with an albino female. This albino female belonged to a hybrid strain derived from strain 139. The first hybrid generation showed no tumor. It has never shown any tumor anywhere throughout the entire stock, which has been bred out in several branches. In the second hybrid generation there is a lympho-sarcoma of the thymus, two spindle-cell sarcomas of the face, two carcinomas of the mammary gland; and again, in the fourth generation, carcinoma of the mammary gland. Up here I have charted some human strains for the interest they may have. In this white strain the tumors are entirely abdominal; in this colored strain where uterine tumors came in on both sides of the family in the later generation no tumors occurred but uterine tumors. It has been said in criticism of that chart that the uterine tumor is the common tumor in the colored race, but I think it would be a fair reply to make to that statement that that is a common tumor in the colored race partly because the tendency to that type of tumor has been so commonly bred in. Here, for example, where it occurs on both sides of the family, it comes out in 3 cases out of 4 in the later generation.

These charts do not represent picked results. They are typical of what has happened throughout my entire work with cancer wherever cancer has been bred in. It has been objected that since inbreeding does not characterize the human race these results have no application to man. Nothing could be further from the fact. The method of the laboratory in getting fixed strains must always be that of inbreeding; there is no other way to tell what went into a cross, but in the matter of the general increase of tumors outbreeding will do far more to increase it than inbreeding could, as you see by all these hybrid strains, for inbreeding if persisted in destroys the strain. This female (No. 529) mated with her brother, never produced any young at all that lived to cancer age; mated with an albino from a nonrelated strain she produced an enormous family, which has been bred out and which has been hybridized into many strains carrying cancer with it. Again, her mother (female No. 293), mated with her brother, produced only three young that lived to cancer age, but mated over here in strain 65, this hybrid chart that I showed you, she produced a large number of progeny and started up a whole line of cancerous mice that has carried cancer into every strain with which it has been hybridized.

It has been suggested also that inbreeding, which weakens the strain, renders it more susceptible to cancer. My cancer strains are strong by every criterion of strength in the beginning. As I have already said, they can be bred out by inbreeding, eventually destroyed by inbreeding, just as every strain of mice that I have ever handled can be destroyed by persistent inbreeding; but in the beginning it is the strong mice, it is the strong strains, which show cancer, and it is the strong members of strong strains that are the individuals that develop cancer.

And this brings me to a few of the points in the etiology of cancer which I wish to suggest. I have found that reduction of feeding to a point which produces general emaciation reduces the amount of cancer in a strain and holds back the neoplastic growth in the individual. I have underway, at the present time, experiments on strains of mice where cancer has practically been starved out by a diet too low to sustain it. Cancer is a disease of middle and late life, when growth processes are largely reproduction and regeneration. Infections are diseases of early life, when growth processes are largely accretions in quantity and in complexity. The most careful experiments in my laboratory have failed to produce the spread of cancer by any of the means which spread any infection common in the laboratory. If one of

the common infections gets into a section of the laboratory, unless the individuals carrying it are immediately isolated, the entire family and all the neighbors will be wiped out, because the infection will spread not only through the cage but through all the adjacent cages. The most careful and long-continued effort to spread cancer in this way has never met with a single case of success. I have had the young of cancer mothers fed and reared from the moment of birth by noncancerous females; I have had the young of noncancerous females fed and reared from the moment of birth by females with exuding cancers of the mammary gland; I have never found that these experiments modified in the least the occurrence of cancer in cancer strains, nor have they introduced it in the noncancer strains.

I find that vigorous growth is necessary for tumor growth. As I have said, the members of my laboratory that showed cancer are the strong members of strong strains. Vigorous growth processes militate against infections. A very slight infection will kill a pregnant female. It is amazing, frequently, at autopsy to find out how very slight an infection has produced death in a pregnant female. This female (No. 5417) who heads strain 338 had her tumor a year before it killed her and during that time she produced six litters of young. I have shown those that lived to cancer age in the charts presented to-night. All these young were born after her tumor. Every mouse in my laboratory that has been strongly reproductive after the appearance of tumor has had the tumor growth greatly delayed during pregnancy and the rearing of young, whereas a young female of vigorous reproductive age, if not mated, will die within about 6 weeks after the appearance of the tumor, the tumor frequently being larger than the mouse itself.

Whatever the ultimate nature of cancer may prove to be, whether infectious or not, it has one quality which no mouse infection that I have handled in the laboratory has, it follows the laws of heredity with an exactness which makes it a character that can be manipulated. It can be bred into strains where it has never before occurred, and it can be drawn out in extracted strains which carry cancer into every line with which they are hybridized and these hybrid offspring of strains where cancer has been bred in will carry cancer again into every strain with which they are hybridized; or it can be bred out of a strain which originally carried 100 per cent of cancer.

Hereupon, the chairman announced the reading of the following papers:

Factors in immunity to cancer, by James B. Murphy and John J. Morton.

Immunity to transplantable neoplasms, by William H. Woglom.

Tumor immunity, by E. E. Tyzzer.

Chemotherapeutic experiments on rat tumors, by Richard Weil.

The application of chemical methods to the study of cancer, by Casimir Funk.

FACTORS IN IMMUNITY TO CANCER.

By JAMES B. MURPHY AND JOHN J. MORTON.

Laboratories of the Rockefeller Institute for Medical Research.

It has been shown in previous communications that the resistance to heteroplastic tissue grafts apparently depends on the activity of the lymphocyte. The facts on which this conclusion is based are briefly as follows: The chick embryo, which normally lacks the ability to destroy a heteroplastic tissue graft, if supplied with a bit

of adult lymphoid tissue, becomes as resistant as the adult in this respect. Furthermore, an adult animal deprived of the major portion of its lymphoid system by repeated small doses of X-ray, no longer has the power to destroy a graft of foreign tissue and this tissue will grow actively. The chief characteristic of a failing heteroplastic graft in the unsuitable host is a marked local accumulation of lymphocytes. The histological picture is identical in a failing cancer graft in an immune animal of the same species. Synchronous with the establishment of the cancer immunity and during the period in which the lymphocytes are accumulating around the cancer graft, there is a lymphocytic crisis in the circulating blood. This is found in the actively immunized animals as well as in those possessing a natural immunity, but is totally lacking in animals susceptible to the cancer graft. If the lymphoid crisis be prevented in immunized animals by a previous destruction of the lymphoid elements with X-ray the potentially immune animal is changed to a susceptible one.

We have noted that while repeated exposures to X-ray will destroy the lymphoid elements of an animal, one small dose will stimulate these same cells. With this artificial method of producing a lymphocytosis we have attempted to study the relation of this condition to the resistance of mice to their own spontaneous tumors. For evident reasons it was necessary to rule out the complicated question of the direct effect of X-ray on the cancer. In order to do this we have removed the cancer at operation and with the cancer out the animal has been subjected to a stimulating dose of X-ray. Immediately after this a graft of the original tumor was replaced in the groin of the animal. As a control the same procedure was carried out, but with X-ray treatment omitted. As a further check to these results cancers of spontaneous origin were removed from a number of animals and in this set the cancers were exposed direct to the same amount of X-ray as the animals in the first group had received. After this a graft of the tumor was returned to the original host.

The results of these three experiments are to be judged by two criteria: First, whether or not there is a return of the disease, either at the site of removal of the cancer, or at the point of inoculation of the returned graft; and, second, the time at which the returned graft starts in active growth, if at all. The figures on these points are given in the following table:

	Immune.	Susceptible.	Local recurrence of tumor.	Average time for appearance of graft.
	Per cent.	*Per cent.*	*Per cent.*	
Series I	50.0	50.0	21.2	5 weeks and 4 days.
Series II	3.4	96.6	48.3	1 week and 5 days.
Series III	.....	100.0	40.0	1 week and 3 days.

Series I was composed of 52 animals with spontaneous cancer treated by X-ray while the cancer was outside of the body, with later a return of a graft of the tumor. Series II was made up of 29 control animals in which the cancer was removed and a graft returned without treatment to either animal or tumor. Series III was made up of 10 animals from whom the cancer was removed and the cancer subjected directly to the same amount of X-ray as the animals received in the first series, and later a graft of this X-rayed cancer returned to its original host.

It will be seen from these figures that an X-ray dose which produced a lymphocytosis when administered directly to the animal was sufficient to render 50 per cent of the mice so treated immune to returned graft of their own tumor and in the other 50 per cent to greatly retard the return of the disease. A similar dose of X-ray given directly to the cancer outside of the body did not influence the subsequent growth of a graft of this tumor when returned to its original host. The contrast between these figures and those of the control series is striking, as is also the number of local recurrences in the two series. If this effect is obtained with one stimulating dose of X-ray it is prob-

able that a more pronounced result might be obtained by a second exposure to X-ray after a suitable interval.

For a comprehensive review of the literature on cancer resistance see:

Woglom, W. H.: The Study of Experimental Cancer. A Review. Studies in Cancer and Allied Subjects. New York, 1913, i, 128.

Murphy, James B.: Transplantability of Tissues to the Embryo of Foreign Species. Jour. Exper. Med., 1913, xvii, No. 4, 482.

——— The Ultimate Fate of Mammalian Tissue Implanted in the Chick Embryo. Jour. Exper. Med., 1914, xix, No. 2, 181.

——— Factors of Resistance to Heteroplastic Tissue Grafting. Jour. Exper. Med., 1914, xix, No. 5, 513.

——— Heteroplastic Tissue Grafting Effected through Roentgen-ray Lymphoid Destruction. Jour. Am. Med. Assn., 1914, lxii, 1459.

Murphy, James B., and Morton, J. J.: The Lymphocyte in Natural and Induced Resistance to Transplanted Cancer. Jour. Exper. Med., 1915, xxii, No. 2, 204.

——— The Effect of Roentgen Rays on the Rate of Growth of Spontaneous Tumors in Mice. Jour. Exper. Med., 1915, xxii, No. 6, 800.

IMMUNITY TO TRANSPLANTABLE NEOPLASMS.

By WILLIAM H. WOGLOM,

George Crocker Special Research Fund, Columbia University.

It is customary to divide immunity into two types, natural and acquired, and to subdivide the latter into active and passive.

Natural immunity to a transplantable tumor is present, as a rule, in old animals, and in species other than that in which the neoplasm primarily arose; thus, with an occasional exception, the transplantable new growths of mice are not transferable to rats. To this statement, however, the following important exception has been discovered. Murphy [1] has shown that the embryo chick is susceptible to rat tumors until about the time of hatching, and that the resistance which supervenes after this period is connected in some way with the maturation of the spleen and the bone marrow. From this point he [2] has gone on to demonstrate that mouse sarcomata will proliferate in rats after the lymphoid system has been injured by exposure to X-rays or by the administration of benzol, for a longer period than in control animals. Hence it appears that the resistance obtaining in foreign species may be abrogated by interfering with the lymphocytic activity.

Under natural immunity may be discussed also the resistance of the spleen to metastatic tumors, and the reputed insusceptibility of the testis to inoculation with a certain neoplasm. Both von Hansemann [3] and Kettle [4] have recently asserted that the immunity of the spleen is not so efficient as had formerly been supposed; and as it is known, furthermore, that grafts of transplantable neoplasms are able to proliferate without embarrassment in the spleen of animals, whatever freedom from metastatic growths this organ enjoys is probably referable, not to an antagonism against the cell higher than that opposed by the other organs, but chiefly to some mechanical factor. Such an explanation has been advanced by the latter of these two authors, who has suggested that the contractions of the spleen force tumor emboli out of the organ again, and even prevent the growth of a large number of those that have become impacted in its capillaries.

[1] Jour. Exp. Med., 1914, xix, 513.
[2] Jour. Am. Med. Assoc., 1914, lxii, 1459.
[3] Deutsch. Med. Wchnschr., 1915, xli, 633.
[4] Jour. Path. & Bacteriol., 1912-13, xvii, 40.

In other words, it is probable that wherever the tumor cell comes to rest in the tissues there it will grow, for no organ in the mouse has proved resistant to inoculation. Even the testis of the rat, formerly said to be almost or quite immune to the Flexner-Jobling carcinoma, has been proved by Woglom [1] to offer very nearly as favorable a soil as the subcutaneous tissues.

However, in comparing natural with artificial metastasis, that is, with inoculation into the various organs, one distinction must not be overlooked; in the former process, the tumor cells come to rest in a blood- or a lymph-channel, while in the latter they are deposited directly in the tissues, where the conditions for growth are much more favorable in many instances; for, as Takahashi [2] has found, the cells of certain tumors are unable to establish vascular connections with the vessel wall soon enough to permit their survival.

One further factor, and an indefinite one, must be taken into account: This is the chemistry of the tissues in which the tumor embolus settles. In how far metastasis is encouraged by favorable chemical surroundings is still an unsettled question, though it can at least be said that this factor does not appear to be as important, in general, as the mechanical influences emphasized by von Recklinghausen and his pupils. On the other hand, it can not be summarily dismissed from consideration.

To recapitulate the essentials of metastasis, it appears that this process is governed by several factors. If a secondary tumor is to be produced, the cells of the primary neoplasm must have the power to establish vascular connections; secondly, they must remain undisturbed in the vessel long enough for the union to be completed; and, finally, if these two conditions have been fulfilled, the organ in which they happen to lie is probably a matter of indifference in the great majority of cases.

Acquired resistance is conferred by unsuccessful inoculation with a tumor or even by treatment with normal tissues. In both cases, however, the cells must be derived from the species of animal which it is desired to immunize. The most potent material is embryo skin, which will effect resistance to carcinoma in nearly 100 per cent of treated animals. The refractory condition so evolved lasts for about 80 days, as Woglom [3] has shown (fig. 1). Less active is kidney, and still less active are emulsions of spontaneous tumor, though the immunity to which the two latter give rise lasts for about the same length of time as that produced by embryo skin.

Acquired resistance to sarcoma has not been so extensively studied, chiefly because this type of neoplasm grows too irregularly to lend itself to such an investigation. The Imperial Cancer Research Fund, however, possesses a mouse sarcoma of fairly uniform growth energy, so that Tsurumi [4] has been able finally to approach the question. He found that mouse embryo skin would immunize against sarcoma also, and that the time and rate of development of the resistant state were about the same as in the case of carcinoma (fig. 2). Sarcomata which were able to grow in spite of attempts to immunize the host, evidently owed this power to their high initial proliferation, for when their cells were damaged by incubation at 37° C. they, too, became susceptible to immunity.

We have tried at the Crocker Fund [5] to immunize fowls against the Rous chicken sarcoma by treatment with chicken embryo, but have been unable to make them refractory (fig. 3). Had the attempt succeeded the result could have been regarded as evidence in favor of the true neoplastic nature of this peculiar growth, but its failure can not be employed to support the opposite side of the argument, and for two reasons. In the first place, it is not even known whether the phenomena of immunity characteristic of the mouse and rat can be duplicated in fowls, and, in the second, the sarcomata, in mice at least, are not so susceptible to artificial resistance in the host, as has been indicated in the preceding paragraph.

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[1] Jour. Exp. Med., 1916, xxiii, 189.
[2] Jour. Path. & Bacteriol., 1915, xx, 76.
[3] Jour. Exp. Med., 1912, xvi, 620.
[4] Jour. Path. & Bacteriol., 1915, xx, 1.
[5] Jour. Exp. Med., 1915, xxii, 154.

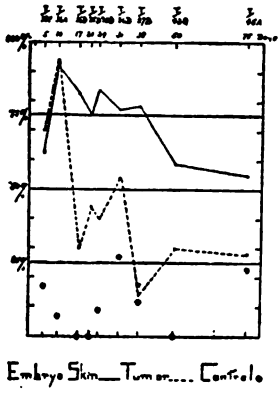


FIG. 1.—Curves showing the extent and duration of the resistance induced in mice with embryo mouse skin and spontaneous adenocarcinomata of the mammary gland of the mouse, respectively.

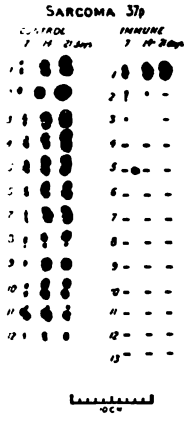


FIG. 2.—Immunity to sarcoma produced by treatment with embryo mouse skin one week before inoculation.

TABLE I.

Experiment No.	Interval between treatment and tumor inoculation.	Dose of embryo emulsion.	No. of chickens.	Tumors.	No tumors.
	days	cc.			
I	5	5.0	20 controls*	10	0
			8 treated	5	3
II	5	10.0	8 controls	6	0
			6 treated	6	0
III	20	5.0	15 controls	15	0
			17 treated	16	1
IV	12	5.0	11 controls	11	0
			10 treated	10	0
V	14	2.0	5 controls	5	0
			9 treated	9	0
VI	14	4.0	2 controls	2	0
			5 treated	5	0
VII	25	5.0	10 controls*	10	0
			11 treated	10	1
VIII	20	2.0	3 controls	3	0
			3 treated	3	0
IX	22	5.0	5 controls	5	0
			2 treated	2	1
X	40	5.0	11 controls	11	0
			7 treated	7	0
XI	70	5.0	22 controls	21	1
			20 treated	18	2
XII	100	5.0	16 controls	15	1
			18 treated	17	0

* Same controls used for both experiments.

FIG. 3.—No immunity to the Rous chicken sarcoma produced by treatment with fowl embryo.

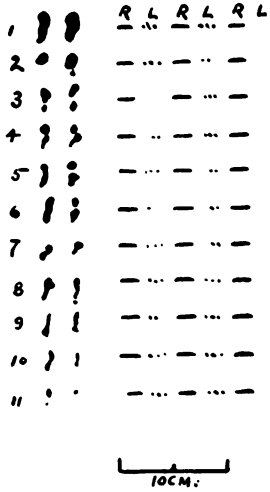


FIG. 4.—Mice in which the tumor to the left has grown for about 10 days, are immune to reinoculation, even after it has been removed. Reinoculations into the left axilla were all negative (—), and the tumor did not recur in the right (—), showing that extirpation was complete. Adapted from Russell's article.

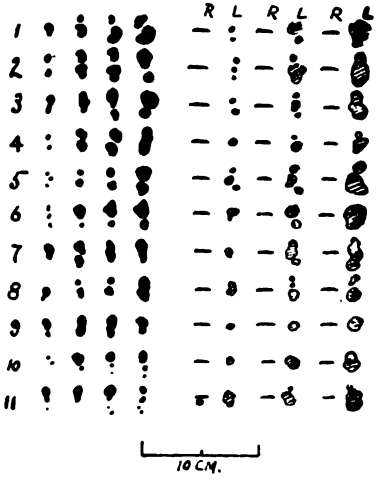


FIG. 5.—The tumor to the left (solid) does not immunize during its growth. The barred tumors are the result of reinoculation in the left axilla after removal from the right of the growths primarily inoculated. Recurrence did not take place (—), showing that extirpation was complete. Adapted from Russell's article.

A type of acquired resistance, first described by Ehrlich, and by him called "athreptic immunity," still remains for discussion. Here the resistance to reinoculation which he found in animals with rapidly growing neoplasms, was referred to a withdrawal from the body of growth stuffs indispensable for the proliferation of tumor cells, and the consequent unfavorable circumstances amidst which the second graft was placed. Russell [1] has demonstrated, however, that there are two distinct types of tumor, one of which immunizes, during its growth, against a second inoculation, the other of which lacks this power. (Figs. 4 and 5.) It is plain, therefore, that those investigators who have substantiated the occurrence of athreptic immunity, have been working with the first type, while those who have been unable so to do have been dealing with the second. A final proof of the identity of athreptic immunity with the ordinary type of acquired immunity was advanced by Bashford and Russell [2] in their demonstration that athreptic resistance depends upon the same factor responsible for other types of immunity—namely, upon the absence of a stroma reaction.

The converse of immunity to transplantable neoplasms is hypersusceptibility, a condition which can be brought about by treatment with body juices or killed tissues. It has been asserted recently that a diet rich in lactose will also produce a state of heightened receptivity, but we have been able to demonstrate at the Crocker Fund [3] that the statement does not hold for the majority of carcinomata. The apparent hypersusceptibility must have been due, therefore, to some one of those experimental errors which it is so difficult to avoid in cancer research.

TUMOR IMMUNITY.

ERNEST EDWARD TYZZER.

Cancer Commission of Harvard University.

In a consideration of tumor immunity it appears desirable to discuss resistance to spontaneous tumors and to implanted tumor separately. Although results obtained with experimentally implanted tumors have contributed to the biology of tumors, these results can not be applied directly to spontaneous tumors, and this is especially true with respect to immunity. It has long been recognized that immunity to implanted tumor gives no assurance against the subsequent development of spontaneous tumors. It is quite impossible to present within reasonable space a comprehensive review of all investigation in tumor immunity, so that in the attempt to furnish an adequate explanation of the phenomena relating to tumor immunity, such data as appear to bear directly on the subject will be discussed and correlated as far as possible.

RESISTANCE TO SPONTANEOUS TUMORS.

The individual who is without any form of tumor may, in a certain sense, be regarded as immune, and the mechanism for regulating the growth of tissue as one of immunity. The normal individual may, however, develop a tumor at any time and, with the limitation of active growth to a relatively small group of cells, it appears improbable that there is any abnormality of the growth-regulating mechanism but rather a local derangement of the group of tissue cells from which the tumor arises. This view is supported in that Haaland has observed that tumors may be transplanted to a normal animal as readily as to one in which a tumor has devleoped and also in that it is found that young healthy animals are more favorable to the growth of implanted tumor than older ones. Since natural resistance, once a malignant tumor

[1] Fifth Sci. Report, Imperial Cancer Research Fund, London, 1912, 1.

[2] Proc. Roy. Soc., Series B, 1909-1910, lxxxii, 298.

[3] Jour. Exp. Med., 1915, xxii, 766.

has become established, appears to be usually ineffective, many attempts have been made to increase it through various artificial procedures.

Spontaneous regression.—Recovery from a tumor which has shown malignant characteristics is rare. A number of such recoveries have, however, been recorded and incomplete excision has in a few rare instances been followed by complete cure. That there is also spontaneous recovery from certain border line conditions appears probable. Evidence of local disappearance of tumor is more frequently met with; for example, a scirrhous carcinoma of the breast may disappear in certain regions while actively growing in others.

Reaction of tissues to tumor.—The histological study of tumors also discloses reactions of the surrounding tissue, some of which are unquestionably favorable, others distinctly unfavorable to the growth of the tumor tissue. Certain uterine carcinomata, for example, excite a pronounced infiltration of eosinophiles, and in such cases the reactionary tissues may exceed in amount the essential tissue of the tumor.[1] Certain carcinomata of the lip, as well as the border line conditions in this region, show marked inflammation in the tissue near the abnormal epithelium, and degenerative changes in the contiguous connective tissue are frequently prominent. In other instances proliferative changes in the supporting tissues are most marked. This is seen in adenomata of the breast and in the papillary tumors of the ovary. The proliferation may be present in such a degree as to give the appearance of mixed tumor or of sarcoma. Such a degree of connective tissue proliferation has attended the transplantation of certain carcinomata in mice as to constitute at first a mixed tumor and later on, after the elimination of the epithelial elements, a sarcoma. Thus Ehrlich, Loeb, and Haaland have each produced sarcomata experimentally by the inoculation of epithelial tumors. With certain carcinomata a dense scar-like tissue is formed, which tends to bring about the atrophy and disappearance of the tumor epithelium through pressure and interference with nutrition. Accordingly, it is possible to distinguish a great variety of reactions on the part of the supporting tissue in response to the influence of tumor cells. Some are distinctly antagonistic, others indifferent, others favorable to the growth of the tumor. It is obvious that unless the neoplastic tissue is of such nature as to stimulate a reaction in some degree favorable to its support and nutrition, its continued growth will be impossible. Such reactions furnish definite evidence of the biological variation of the tumor from the somatic tissue from which it arises, a subject which will be further discussed later on.

Relation of resistance to metastasis.—In the distribution of metastasis there is considerable evidence of organal immunity. Certain organs may be free from secondary tumors in cases in which there is every indication of a general dissemination of the tumor cells, and emboli of tumor cells have been found undergoing degeneration. Certain tumors are widely distributed in certain tissues—for example, lymphomata which grow profusely throughout the lymphoid tissue—while other tissues are for the most part exempt from invasion. On the other hand, epidermoid carcinomata are observed which, while infiltrating the tissues diffusely, are at the same time being reduced to inert masses of cornified epithelium wherever their cells have lodged in the lymph-nodes. However, on the whole, it is impossible to ascertain in most cases whether the distribution of the tumor is determined by its biological peculiarities with respect to the invasion of vessels or by the unfavorable conditions furnished it by certain organs and tissues. Adequate vascularization is probably an essential factor in the nutrition of most tumor metastases. A more definite knowledge of the principles governing organ or tissue exemption from metastasis will be acquired when the experimental method is more generally applied, and animal tumors, since they are available in considerable numbers, are suitable for this problem.

[1] Noted in a case from the collection of the Department of Pathology, Harvard Medical School; also noted by Mallory.

The opinion has been expressed that metastasis is to some extent governed by the resistance of the individual. Sticker recognizes a premetastatic period in the growth of tumors during which the resistance of the body is sufficient to destroy all cells which may enter the circulation. Gay, on finding that a certain proportion of rats bearing the Flexner-Jobling tumor recovered if reinoculated during this period, adopted Sticker's views views in the explanation of his results. The author has found that by the forcible manipulation of a tumor of the Japanese waltzing mouse, metastases may be produced experimentally, and it is not only possible in this way to reduce artificially the premetastatic period, but also, by ascertaining the time required for the tumor emboli to become visible nodules, to show that the natural premetastatic period is actually considerably shorter than it had appeared. It has been repeatedly shown that animals, on developing tumors from transplants, frequently become more unfavorable to the growth of subsequent implants. Although it is not improbable that the presence of a local tumor may stimulate a reaction which is unfavorable for the development of tumor emboli, experimental evidence of this is lacking, and the peculiarities of the individual tumor with respect to its ability to disseminate its cells should be taken into consideration. Tumors which metastasized in the individuals in which they originated have a greater tendency than others to metastasize during propagation.

Certain points with respect to conditions governing the growth of tissues are readily determined in human beings. The following observations were made with respect to the persistence of transplants of the abnormal tissue in myelogenous leukemia and Hodgkin's disease during the course of certain procedures that were undertaken by the members of the staff[1] of the Huntington Hospital with the view of testing the efficacy of autologous vaccinations which was at that time on trial in the treatment of tumors.

Myelogenous leukemia.—Case C. I. 12. 5. This patient, a woman 37 years of age, showed marked enlargement of the spleen and a white count varying from 91,000 to 496,000 while under observation; duration at least two years.

June 3, 1912. A cubic centimeter of leucocytes collected from citrated blood was injected subcutaneously.

June 5, 1912. Slight tenderness and induration at site of inoculation. This had entirely disappeared at the time of the next observation several days later.

Larger quantities of leucocytes were employed in subsequent injections—15 cubic centimeters being used in one instance—but these were always quickly absorbed.

June 29, 1912. One cubic centimeter of blood was drawn from a vein and injected immediately beneath the skin of the upper arm.

June 30, 1912. The blood has been almost wholly absorbed and there was no discoloration present.

Hodgkin's disease.—Case I. 12. 43. A girl, 17 years of age, with enlargement of the glands of the neck, axilla, and mediastinum; duration of disease, 4½ years.

March 10, 1912. A small nodule was excised for diagnosis. A small portion of this was immediately inoculated subcutaneously near the insertion of the deltoid muscle by means of a trochar. Following this the implant was palpable and the overlying skin slightly reddened.

March 13, 1912. No reddening and the implant had diminished in size.

March 19, 1912. No trace of the implant remained.

These observations show that the abnormal cells in these two diseases do not find the conditions furnished by the subcutaneous tissues favorable for their development.

Diagnostic tests and curative sera.—A considerable portion of the work on immunity to spontaneous tumors has been done in connection with human cases and falls naturally into two divisions; first, the reactions which might serve as diagnostic or prognostic tests, and second, measures which have been carried out with the view of effecting a cure by some general form of treatment. Among the proposed diagnostic methods may be mentioned Freund's reaction, the meiostagmin reaction, the hemolysis test, Abderhalden's test, the cobra venom test, and complement fixation. As

[1] Thomas Ordway, Ellis Kellert and the author.

possible curative agents, trypsin, sera from resistant human cases, living tumor used as an autologous vaccine, tumor extracts and cell ferments, dried animal tumors, and the transfused blood of normal individuals have been employed. Since the various tests each require separate consideration no discussion of them will be undertaken. It is notable, however, that up to the present time these have in general been found either unreliable or unpractical. The general failure of the long list of therapeutic measures for which claims have been made is also a matter of common knowledge.

IMMUNITY TO TRANSPLANTED TUMOR TISSUE.

The subject of immunity to transplanted tumor tissue has been extensively investigated. Although the transplanted tumors of rats and mice are especially favorable for experimentation, there has been more or less discrepancy in the results obtained by different investigators. Explanation for this is found both in differences in the biological character of the various tumors employed as well as in differences in the character of the animals with which these are tested. Russell has employed in his investigations a great number of tumors, the immunizing qualities of which he has determined by testing them upon mice of the same breed with adequate controls with respect to age and weight. The author has attacked the problem from the diametrically opposite side and has tested the reaction of different varieties of mice to a single tumor. Thus while in the experiments of one a stock of tame mice was taken as the indifferent or constant and the tumor as the variable factor, in the experiments of the others a single tumor served as the constant and different varieties of mice and their hybrids as the variables.

General features.—Immunity to transplanted tumor has as its basis the reaction of the organism to a foreign cell. It has been shown that animals treated with normal cells may manifest an increased resistance to implanted tumor and also that animals treated with tumor tissue may subsequently show pronounced immunity to the same tumor or to other tumors. The condition of resistance to implantation of various types of tumors by the previous injection of a single tumor has been termed panimmunity by Ehrlich. Differences in the immunizing qualities of various tumors has been definitely established by Russell, who has found that in general the poorly growing tumors serve as the more "efficient antigens." Loeb, Haaland, and the author have each shown that tumors may be readily reimplanted in the individuals in which they arise—autoplastic grafting. When a tumor is transferred to other individuals of the same race, a variable number of failures of growth usually occur. and greater difficulty is encountered in the successful implantation of tumor tissue in other races and varieties—homoiolastic grafting. Practically invariable failure follows the implantation of tumor in other species—heteroplastic grafting. The degree of the immunity which develops thus depends apparently on the foreignness of the immunizing cell with respect to the organism into which it is introduced. The more foreign cells accordingly serve as the more effective and the more closely related cells as the less effective antigens.

Antigen.—Immunity to tumor tissue is evidently excited by some subtle product of cell metabolism eliminated in small amount, but over considerable periods of time. Repeated attempts have been made to immunize with dead tumor or other tissue products, but notwithstanding several unconfirmed reports of success such procedures have in general proved unsuccessful. The great majority of those who have investigated the subject have thus found that the injection of living cells is essential in the production of immunity. While such treatment may serve to prevent the growth of subsequently implanted tumor, it does not bring about the retrogression of established tumors. The regression of implanted tumors of large size may, however, occur spontaneously, and the animals are then immune to further implantation. Tumors have been found which grow in practically 100 per cent on implantation but which subsequently all retrogress if left for a sufficiently long time.

Histology of the tissue reactions to transplanted tumor.—When a tumor such as the carcinoma (J. w. A.) of the Japanese waltzing mouse is implanted into a series of common mice—i. e., into individuals of an alien race—its continued growth is invariably prevented. If these mice are killed at different intervals after inoculation and a histological study is made of the implants and the surrounding tissue it is found that the tumor grows for a period of six or seven days as readily as in the Japanese waltzing mouse, the variety in which it originated and in which implants invariably continue to grow. During this time the common mouse provides stroma and blood vessels for the implant. At the end of this period, an inflammatory reaction appears, evidently as the result either of a slight injury to the surrounding tissue or of some chemotactic substance, and the cellular exudate accumulates in amount sufficient to interfere with the blood supply and to isolate the tumor from all healthy supporting tissue so that its destruction is accomplished. If common mice in which this reaction has taken place are subsequently reinoculated with the same tumor, the inflammatory reaction appears several days earlier and the implant is thus disposed of much more promptly than in similar untreated common mice. Such nonsusceptible common mice are not, therefore, strictly speaking, naturally immune, but develop an immunity which first manifests itself six or seven days after inoculation. They thus develop a quality not present in the untreated mice, in other words an active immunity.

Nonsusceptibility versus immunity.—To ascribe nonsusceptibility to "natural immunity" is confusing, if not inaccurate, for there is ample evidence to show that this quality is based on an ability to acquire, under artificial conditions, an active immunity. Russell states that the natural resistance of animals may be considered as nothing more than an ability to develop readily an active immunity. It appears preferable to use the terms nonsusceptibility and susceptibility, the former to indicate ability to develop effective immunity to a given tumor so as to make its continued development impossible, the latter to indicate failure to develop effective immunity in response to an implant of tumor. The two terms find application with respect to both individuals and races. While Japanese waltzing mice furnish an example of an uniformly susceptible and common mice of an uniformly nonsusceptible race, with respect to a single tumor, with other races and other tumors varying proportions of susceptible and nonsusceptible individuals are found. There are various degrees of susceptibility, and this character is also subject to variation in individuals, since certain animals in which tumor implants would ordinarily grow may be rendered immune and thereby nonsusceptible by the injection of normal tissue or poorly growing tumor. Other animals which are nonsusceptible may be made nonresistant through appropriate treatment.

Hypotheses in explanation of tumor immunity.—Since active immunity to implanted tumor is recognized as an established fact, the question next arises as to the nature of this immunity. A number of hypotheses have been offered in explanation.

The body fluids of immune mice have not been observed to have any direct cytolytic action on tumor cells either in the test tube or in the body of the immune animals. Immunity to homoioplastic implants thus appears to differ from that produced by the injection of the tissue of a foreign species in which cytolysins, precipitins, opsonins, etc., are readily demonstrated.

The possible importance of intercurrent bacterial infection in tumor immunity has been emphasized by Pitzman, who claims that infected tumors confer protection, whereas noninfected tumors do not. This is not in accordance with many well established facts, and it is especially difficult on this basis to account for the constant appearance of an inflammatory reaction around implants in one variety and its absence around implants in parallel series of another variety of mice. It is likewise difficult on the hypothesis of immunity through concomitant infection to explain the occurrence

of an inflammatory reaction only around living tumor, its prompt subsidence as soon as the latter becomes wholly necrotic, and also the failure of necrotic tumor to produce immunity. In order to put this hypothesis to further test a tumor infected with a nonpathogenic bacillus was ground in salt solution and filtered through filter paper. The filtrate was inoculated subcutaneously into a series of mice and later these, together with an equal number of controls, were inoculated with tumor contaminated with the same bacillus. Implants taken twenty and twenty-six hours after inoculation showed in the treated mice more polymorphonuclear leucocytes in foci around the tumor than was the case in the controls. After 48 hours, however, the implants in the treated animals showed practically no infiltration and were developing under more favorable conditions than the controls. These findings are not, therefore, in accord with the view that tumor immunity is brought about through bacterial infection.

Athrepsia, or deficiency on the part of the body fluids with respect to certain substances essential for the nutrition of the tumor, fails to account for both the vigorous temporary growth in nonsusceptible animals, and also the inflammatory reaction which precedes the destruction of the tumor.

The hypothesis that something is produced in the immune animal which renders inert the products of the tumor and so inhibits the proliferation of stroma and blood vessels has been advanced by Russell and others. While this would not account for the retrogression of large established tumors, we have no evidence to disprove that this mechanism applies to certain cases in which there is no active inflammatory process about the implant. Theoretically it would appear quite probable that, in instances where the tumor cells were less foreign in nature, the immune body produced may call forth no excessive reaction on the part of the host tissue and nevertheless be sufficient to inhibit the stimulating effect of the tumor on the growth of blood vessels and connective tissue.

From the observations already alluded to it appears evident that a large proportion of tumor implants in nonsusceptible mice are at first provided with both stroma and blood vessels, but later on become isolated from healthy supporting tissue by an inflammatory reaction manifested by abundant cellular exudation and degenerative changes in the tissue around the tumor. This delayed reaction of the host tissue is difficult to explain except on the hypothesis that an immune body has been produced. Since there is no available evidence indicating the plurality of immune substances in tumor-immune animals, and in view of the failure to demonstrate lysins, precipitins, or any of the recognized immune bodies, it appears justifiable for purposes of discussion to speak of the protective material present as a single substance or immune body. With an immune body present, the tumor products are rendered strongly chemotactic so that the surrounding tissue, as well as the implant, becomes infiltrated with leucocytes. The reaction is not merely exudative in character but is proliferative as well, for there is a great increase in the number of fibroblasts in the surrounding tissue, and these increase in size as in granulation tissue. That others have attached so great importance to lymphocyte infiltration may be due in part to difference of material, to the period at which the process was studied, or to a failure to recognize all the constituents of the reaction. From both the material on which the present study is based, and from the illustrations of other authors, it is evident that we have in general to deal, not with an infiltration of a single type of cell, but with an inflammation which may vary somewhat with the material, though more especially with its duration. Thus in immunized mice the reaction is more prompt and polynuclear leucocytes are more numerous, while in untreated nonsusceptible mice the reaction appears later—not earlier than the seventh day—and here the lymphocytes occur in greater numbers. In both instances the reaction manifests itself in the formation of granulation tissue in which proliferative as well as exudative activity is evident.

The pale staining and vacuolation of the cytoplasm, the swelling of the nuclei, and the absence of cell division are taken as indices of degeneration in the tumor epithelium. Such degenerative changes are of frequent occurrence in implanted tumor epithelium, even in susceptible animals, and they usually occur in those portions of the epithelium farthest from the host tissue, i. e., from the source of nutrition. From the fact that the features of tumor cell degeneration are the same in both susceptible and immune animals, from the gradual progress of this degeneration, and from the visible evidence of a reaction which tends to isolate the tumor from healthy tissue, it is evident that the destruction of the tumor is accomplished by the formation of an immune body which modifies the response of the host tissue.

The number of lymphoid cells in the inflammation around the tumor implant was regarded as significant by Da Fano, who has concluded that it is through the agency of the lymphocytes that immunity is produced. Murphy has arrived at similar conclusions after having found that a rat tumor may be grown in chick embryos in the absence of lymphoid tissue, and that the introduction of certain adult tissues, such as spleen or lymphnode, is sufficient to prevent this. Baeslack has shown a relative increase in the number of lymphocytes in the blood in the course of the retrogression, and a relative decrease during the active growth of tumors. Murphy and Morton, who have made a study of the blood counts in artificially immunized, naturally nonsusceptible, and susceptible mice, have also demonstrated a very marked absolute increase in the number of lymphocytes during the retrogression of implanted tumors. In neither of these articles has the possibility of differences in the leucocyte content of the blood of the tail vessels and that of the heart in rats and mice been discussed. That the white count from the blood of the tail vein may vary within wide limits has been pointed out by Klieneberger and Karl, and this has been the experience of the author. Since the white count of the blood of the tail vein may vary more than 100 per cent and is usually much higher than that of the heart's blood, and since differential counts show that the lymphocytes are approximately 20 per cent more numerous in blood from the tail, the indicated increase in the number of lymphocytes in the blood of immune mice is probably greatly exaggerated. The charts presented by Murphy and Morton show no increase in the lymphocyte count of the immunized mice except on the introduction of tumor tissue. Thus the lymphocyte count in the immunized mouse is shown at precisely the same level before and after the immunizing injection, and yet it would not be denied that an animal so treated now possesses qualities which were previously absent, or, in other words, had become immune—a point of considerable significance. This, together with the fact that these authors were able to lower the resistance of immunized animals by exposure to the X-rays, which are known to have a destructive action on lymphoid cells and other leucocytes, lends additional support to the hypothesis already outlined—i. e., that resistance to transplanted tumor is dependent upon (1) the presence of an immune body which, in the presence of the tumor, either produces injury or otherwise renders the implant chemotactic, and (2) an ability of the tissues to respond to this with an inflammatory reaction which isolates and destroys the implant.

Although it may be possible by repeated X-ray radiation in appropriate amounts to render both naturally nonsusceptible and artificially immunized animals favorable for the growth of implanted tumor, there is in the physiological mechanism thus destroyed nothing specific to tumor immunity. It is inconceivable that there should be sufficient differences in the lymphocyte content of various classes of mice to account for their differences in susceptibility to a given tumor. In fact, other publications by one of these authors tend to show that X-ray radiation tends to lower resistance to a variety of disease-producing agents. The X-ray may evidently destroy the ability of the organism to respond to a certain type of injury with a corresponding type of inflammatory reaction and, applied to tumor immune animals, it in this way decreases their resistance.

It thus appears most probable that at least three factors are concerned in the process of the elimination of implanted tumor. First, antigen, which diffuses from living tumor cells; second, antibody, which in the presence of antigen renders the implant positively chemotactic; and third, in response to this, an inflammatory reaction. With the formation of this immune body tumor products which had previously produced a mild proliferation of the surrounding host tissue are now made strongly chemotactic to leucocytes, and probably slightly injurious to the surrounding tissue. Whether another substance such as complement is necessary in this reaction has not been demonstrated. With the material at hand there is no evidence of a specific chemotactic influence on the lymphoid cells, for different varieties of wandering cells are attracted and other cells stimulated to proliferate. The character of the inflammatory reaction varies here as elsewhere, both with the degree of excitation and with the duration of the process. The lymphoid cells preponderate in the milder and more prolonged reaction, polymorphonuclear leucocytes and endothelial phagocytes in the more prompt and pronounced reactions, and the reaction of the connective tissue is also an important factor.

Passive immunity.—Following the recognition of the immunity of mice in which large implanted tumors had retrogressed, attempts were made to produce passive immunity and through the use of the serum of such immune mice to cure other mice of their tumors. Although success was at first reported, a further trial of such supposedly immune serum was attended with no more frequent retrogression than occurred naturally. In the light of the difficulty in curing established tumors, it is remarkable that no greater effort has been made to demonstrate passive immunity with respect to subsequently implanted tumor. While Gaylord, Clowes, and Baeslack found that the treatment of mice with immune serum appeared to have the effect of lowering the number of takes from subsequent implants, Weil found that the similar treatment of rats with immune serum failed not only to influence the growth of established tumors, but also to prevent the growth of subsequent implants of sarcoma. He was also unable to demonstrate the presence of an immune body by passive sensitization of guinea pigs with the serum of tumor-immune rats. In this instance both the immune plasma and the tumor were derived from a single species, the rat, so that less pronounced results might be expected than in immunity to a foreign proteid. In fact, these results are not inconsistent with the presence of an immune body which influences the reaction of the host but does not directly destroy the tumor cells. It has appeared probable that by histological study reactions may be detected which are not demonstrable in the gross phenomena attending the experiment. The object of the following experiment was to ascertain whether the injection of immune serum at the time of the implantation of tumor in susceptible mice would prevent or in any way influence growth and also whether this in any way modified the reaction of the host tissue to the implant:

With a view of conferring a passive immunity to carcinoma J. w. A on Japanese waltzing mice, an immune serum was obtained from nonsusceptible mice which had been previously immunized by implants of Japanese waltzing mouse tumors. The group of nonsusceptible mice employed consisted of eight F_2, two F_3, and seven F_4 hybrids which had been inoculated on July 27, 1915, with sarcoma J. w. B with negative result. These were inoculated again on October 11, 1915, with carcinoma J. w. A. On bacteriological examination of this tumor no organism was found either in smear or culture. Fifteen days later (Oct. 26) the blood of these mice was collected and defibrinated. With the exception of one mouse which showed a consolidation of a portion of the lung, all appeared in a healthy condition. The blood was kept at a low temperature for about one hour, then centrifugated and the serum used immediately. That the serum was somewhat tinged with red may possibly have been due to pooling the bloods of so many animals.

October 26, 1915. Thirty-six Japanese waltzing mice were employed for the test and these were grouped in three series and treated as follows:

Series I. Twelve controls each received an implant of tumor J. w. A. beneath the skin just posterior to the fore leg.

Series II. Twelve mice received each a subcutaneous injection of 0.3 c. c. of the immune serum and immediately following this an implant of tumor J. w. A. The serum was injected into the back just anterior to the tail, while the tumor was implanted behind the fore leg as in the controls.

Series III. The bits of tumor used to inoculate the remaining 12 mice were first placed for about one hour in the small amount of serum left over from the preceding series.

At fixed intervals an animal from each of the three series was killed in order to obtain the tissues for histological study. Six from each series were killed and the others left to observe any differences in the growth of the implants. (A nonpathogenic bacillus was found in cultures from the tumor here employed.)

Although the implants were smaller at the end of the first week in certain mice of the two series in which immune serum was used, the subsequent rate of growth of the tumor was more rapid in these than in the controls, so that at the end of four weeks all were larger than the largest tumor of the controls series. Since the numbers were small, these results are only significant in showing that the immune serum administered at the time of implantation did not prevent the development of the tumor in susceptible mice, and that after a short interval it may have had a stimulating rather than a retarding effect on its growth.

No marked histological differences in the reaction of the tissues of the animals of the control series and of those which had received serum-soaked tumor were observed. Readily distinguishable differences with respect to reaction to the tumor implant were noted, however, in the animals treated with immune serum. The tumor epithelium of the 24 and 26 hour implants in the serum-treated series showed few mitotic figures, although these were numerous in the control implants at this time. There was in all implants of the treated animals an extensive degeneration of the tumor epithelium and the living remnants were scattered in isolated islands, whereas in the controls the living tumor formed a more or less continuous peripheral layer. The swelling, pale staining, and vacuolation of cells may be taken as evidence of degeneration, since such changes are ordinarily found in the living portions of implants bordering on the necrotic interior and farthest from the source of nutrition. Although the degeneration of the implanted tumor in the treated mice appeared to be of the same general character as in the untreated, it was more pronounced in the former, and this difference with respect to the extent of the degeneration increased for at least five days. Infiltration of the interior of the implant with polymorphonuclear leucocytes appeared early—26 hours—and persisted for at least four days. The interior of the control implants, although necrotic, was not in any case markedly infiltrated. For three days the amount of collagen in and around the implants was the same in all three series. There was, however, a marked excess of this material within the four and five day implants of the serum-treated mice. The tumor appears to require a somewhat cellular connective tissue for its growth, and the abnormal intercellular substance which appeared in the serum-treated mice was evidently unsuitable in this respect.

From these observations it is evident that the injection of immune serum modified the reaction of the tissues of the implant and host, although not sufficiently to prevent the later development of the tumor. It is possible that the immune serum injected contained a constituent which was slightly toxic for the tumor epithelium, as was indicated by the absence of mitotic figures for a time, and by a degeneration which continued for several days, although it is to be noted that similar degenerative changes were commonly found in portions of implants at a distance from the source of nutrition. It is clear, however, that the immune serum has rendered the implant, especially its necrotic and degenerating portions, positively chemotactic to polynuclear leucocytes. Appearing somewhat later (four days after inoculation) there was an increase of collagen within the implant, and phagocytic cells also appeared. The implanted tumor thus encountered in the serum-treated animals conditions which, although transitory and not sufficient to accomplish passive immunity, were never-

theless definitely unfavorable to its development. It should be noted that the transplantable tumor for which the immune serum was prepared encounters conditions in the Japanese waltzing mouse unusually favorable for its growth so that it is not improbable that effective passive immunity with respect to subsequently implanted tumor may be produced by employing other material.

Specificity.—The fact that blood and other normal tissue may be employed as well as tumor tissue in the production of immunity to the latter indicates that there is no marked degree of tissue specificity in the immunity which develops, but it is probable that there is a considerable degree of racial specificity with respect to the genetic origin or foreignness of the antigens. That certain tumors, however, show greater differences in their immunizing qualities than the embryonic tissues from which they have arisen will be shown later on by the results obtained in the transplantation of hybrid tumors to the parental stocks.

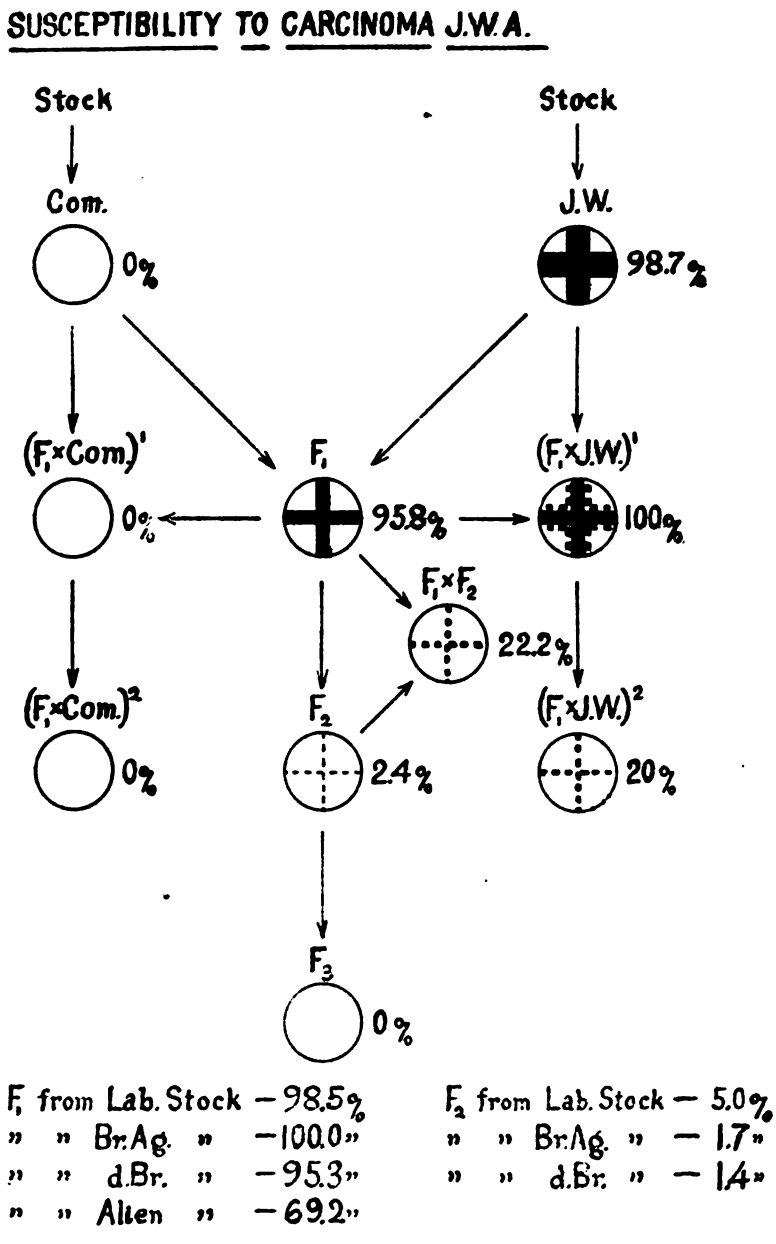
Foreignness of tumor with respect to host a requisite of tumor immunity and an explanation of the inheritance of susceptibility to implanted tumor.—A carcinoma which originated in the Japanese waltzing mouse is found to grow in practically every individual of this variety in which it is implanted. On the contrary it fails to grow in every instance on implantation in the common mouse. By cross-breeding these two varieties successive generations of hybrids have been obtained, the first of which has been back-crossed with both parent stocks. The results obtained from the implantation of this tumor into mice of the various filial generations, and into mice derived from all other matings, are shown in the accompanying chart. The susceptibility of each class has been tested by the simultaneous inoculation of comparative series of mice with a single tumor. The material here considered collectively includes that which has been previously presented by the author, as well as that collected recently in collaboration with Little.

It is quite apparent from these data that susceptibility is not inherited as a single mendelizing factor, for both in the successive filial generations and in the back-crosses between the first filial generation and the parent stocks, the results do not furnish a ratio characteristic of single factor inheritance. There is no blending inheritance, for the results are not intermediate but correspond closely with those obtained in one or the other of the parent stocks. The only hypothesis upon which we can explain these results is, that susceptibility or nonsuscepibility is dependent upon the presence of a complex of independently inherited unit factors. Upon the number of factors necessary for susceptibility will depend the results obtained in the second filial generation. If a few factors are necessary, a condiserable proportion of the indivudals of this generation should prove susceptible; if a larger number of factors are necessary, then a smaller proportion of the individuals of this generation should be susceptible. In the F_1 hybrids, all the inheritable factors of each parent will presumably be present in a single representation. On the principle that these factors will be segregated in the germ cells of this generation, it is possible to compute the results of the random combination of any number of factors which will occur in the mating of the F_1 animals. Although the nature of the material employed makes large numbers requisite for an accurate estimation of the number of factors involved, the results obtained indicate that susceptibility to this tumor is dependent on the presence of a large number of independently inherited factors. Our results with the two stocks of common mice recently employed are such as would be obtained if the presence of from 12 to 14 such factors were necessary for susceptibility.

The effect of a single representation of factors on susceptibility.—Although the factors from both susceptible and nonsusceptible parent stocks must necessarily be present in the F_1 hybrid, it is apparent that those necessary for susceptibility, although here only singly represented, are in the greater part of our material as effective as when doubly represented in the Japanese waltzing mouse. Conversely, the factors necessary for nonsusceptibility, although all present in the same F_1 hybrids, are ineffective

when singly represented or in half dose. That this will not hold true in the cross-breeding of every stock of the common with the Japanese waltzing mouse is clearly indicated in certain earlier experiments. The difference between the percentage of

CHART 1.



positive results obtained in the F_1 hybrids and in the Japanese waltzing mice in recent experiments might possibly be attributable to faulty technic, since only one F_1 animal (1.6 per cent) failed to grow the tumor. In a previous investigation a

slighty higher proportion of failures occurred, and the fact that most of these were in F_1 hybrids ("alien" F_1 hybrids) which were derived from another stock of common mice indicates that a single representation of the factor complex of nonsusceptibility may in some instances prove effective. The nonsusceptibility of certain of these negative F_1 hybrids was established by the negative results of reinoculation.

The effect of single representation of factors on the rate of growth.—Notwithstanding the presence of the factors of nonsusceptibility in the F_1 hybrid, the rate of tumor growth is usually more rapid than in the Japanese waltzing mouse. This fact was established in the earlier experiments by weighing the tumors after equal periods of growth in comparative series of mice. Subsequent experience has also shown that the tumor grows, on the average, more rapidly in the F_1 hybrids. It is probable that this increase in the rate of tumor growth is due to certain factors furnished by the nonsusceptible parent stock. While we are unable to recognize the individual factors concerned, it might be expected that the more rapidly growing and larger hybrids supply the tumor with more abundant nutrition than is the case with the more slowly growing and smaller Japanese waltzing mice. It is found, however, that the tumor grows more rapidly than in Japanese waltzing mice, not only in young growing but also in full-grown F_1 hybrids. The presence of certain singly represented factors of nonsusceptibility evidently calls forth a greater growth of stroma and blood vessels, so that they in this way appear to have a stimulating effect on the growth of the tumor. The injection of the serum of immunized mice also has been shown to have a transitory retarding, but a later stimulating, effect on the growth of tumor J. w. A. in the susceptible Japanese waltzing mouse.

Factor representation in retarded growth.—Although in recent experiments, 3 of 183 hybrids of the second filial generation have shown progressively growing tumors, the rate of growth has been much slower than in the Japanese waltzing or F_1 hybrid mice. From this it appears probable either that not all of the factors found in the Japanese waltzing mice are present even in a single representation, or that certain of the factors of nonsusceptibility become effective through double representation in these positive F_2 mice, for otherwise there is nothing to account for a rate of growth so comparatively slow. In addition to these individuals in the F_2 generation in which the tumor grew progressively, there were certain others in which the tumor grew for a time, but eventually disappeared. For these it is necessary to assume a still more limited representation of certain factors with a correspondingly greater representation of others.

These results having been interpreted from the viewpoint of genetics, it is now important to consider them in the light of what is established for tumor immunity. It has already been pointed out that nonsusceptibility of a class of animals to implanted tumor is to be regarded as an ability to acquire an active immunity, and, conversely, susceptibility as an inability to develop active immunity to a given tumor. If a single tumor be employed as a constant with which to test various groups of mice, it may be found that the race in which it originated is susceptible whereas another race is nonsusceptible. Nonsusceptibility is thus based on foreignness or unlikeness with respect to races, so that when the tissue of one is introduced into the other active immunity is developed. The science of genetics has already established a series of independently inherited unit factors for a considerable number of species, including the mouse. In the consideration of foreignness or unlikeness, what else could be possible than that, in the comparison of individuals or races, some should differ with respect to few factors and others with respect to many factors? Thus the conception of foreignness or unlikeness not only furnishes a basis for tumor immunity, but also makes more comprehensible the inheritance of susceptibility to implanted tumor.

Foreignness as a basis of certain biological differences in tumor.—If groups of mice of known character are used as constants with which to test various tumors, differences

in the behavior of the latter are detected, even though they may have arisen in a single inbred race. It assists materially in the explanation of results if these biological differences are recognized. Certain tumors occur which are transplantable in only a small proportion of cases, even in closely related animals. The conditions requisite for their growth are rarely found apart from the individual in which they arise, i. e., a slight degree of foreignness on the part of the host tissue is fatal to them. For other tumors fewer conditions or factors are necessary, and such, since they are able to withstand a higher degree of foreignness on the part of the host, develop on transplantation in a greater proportion of cases. Such differences in the capacity of a number of tumors for growth in various classes of mice are shown in the following table.

CHART 2.

Tumor.	Common tame mouse.	Japanese waltzing mouse.	F_1 hybrid.	F_2 hybrid.	F_3 hybrid.	(F_1×Com.) hybrid.	(F_1×Com.)[2] hybrid.	(F_1×J.w.)[1] hybrid.	(F_1×J.w.)[2] hybrid.	(F_1×F_2)[1] hybrid.	Remarks.
Common mouse, carcinoma (Jensen).	± 9+ 1−	− 9−	∓ 9− 1+								Differences in susceptibility of various races of common mice noted but data not included.
Common mouse, carcinoma (Ehrlich).	± 15+	∓ 5− 3+	+ 5+ 5−								Differences in susceptibility of various races of common mice to Ehrlich tumor also noted.
Japanese waltzing[1] mouse, carcinoma (J. w. A.).	− 147−	± 893+ 12−	± 126+ 2− (Allen) 9+ 4−	∓ 237− 6+	− 71−	− 78−	− 34−	+ 63+	∓ 4− 1+	∓ 7− 2+	11 of 12 negative J. w.'s not reinoculated. 3 of alien F_1 hybrids not reinoculated.
Japanese waltzing[2] mouse, sarcoma (J. w. B.).	−	+ 185+	+	∓							Susceptibility of other classes to this tumor now under investigation so that data are not included.
Japanese waltzing mouse, sarcoma (J. w. G.).		+ 28+									
F_1 hybrid carcinoma (H. F.).[2]	− 8−	− 13−	∓ 12− 3+ (Allen). 4−	− 11−							Subsequent implantation of carcinoma J. w. A. (9), Sarcomata J. w. B. (7) and J. w. G. (5) in the same J. w. mice was successful in every case. 4 negative F_1 hybrids were found susceptible to Sarcoma J. w. B.
F_1 hybrid carcinoma (H. D.).		− 5−									
F^2 hybrid carcinoma (H. D.).	− 5−			− 14−							
(F_1×Com.)[1] hybrid carcinoma (H. G.).[2]	− 11−	− 11−									This tumor evidently produces no immunity to Sarcoma J. w. B., which grew in 4 of these J. w. mice subsequently inoculated.
Hybrid? (presented by Dr. Gaylord) carcinoma (H. C.).		− 9−		− 6−							

[1] See references Tyzzer, and Little and Tyzzer.

[2] Now under investigation by the same authors.

The biological difference or foreignness of tumors with respect to one another and to the normal somatic tissue from which they arise, is a point of considerable significance. To illustrate: A tumor (H. F.) which arose spontaneously in an F_1 hybrid has been implanted into other individuals of the same generation, and into the parent stocks of common and Japanese waltzing mice. Now, the animal in which this tumor appeared grew as an embryo upon the uterine mucosa of its common mother, without the appearance of any incompatibility between the embryonic and maternal tissue. Since the tumor which has arisen from the somatic tissue of this mouse fails to grow in either of the parent stocks, it would appear probable on this basis that it differs from the soma with respect to its ability to grow on a given soil. Loeb, however, has already called attention to the absence of antagonistic reaction in utero between the maternal and the somewhat foreign embryonic tissue. This F_1 tumor appears to have required factors for its growth which were not all furnished by either the common or the Japanese waltzing mouse nor by all F_1 hybrids. It might be expected that in the cells of this tumor, as in other somatic cells of the F_1 hybrid, there would be an equal representation of factors of both parents. The only alternative would be to consider the hybrid tumor as a manifestation of mosaic inheritance and thus corresponding more closely in its character to the soma of one or the other parent stock. If such were the case, however, it would be expected that this tumor would grow in one of the parent stocks, at least as well as in the F_1 hybrids, but the results are otherwise. The Japanese waltzing mice in which it failed to grow were all found to be susceptible to tumor J. w. A., J. w. B., or J. w. G., so that its failure is to be attributed to feeble growth power—i. e., inability to grow in the presence of even a few foreign factors, rather than to any unusual immunizing property.

Another tumor (H. G.) which arose in a back-cross hybrid from the mating of an F_1 hybrid with a common mouse, failed to grow in common as well as Japanese waltzing mice, although closely related to the former.

Differences in behavior with respect to transplantability are found not only in tumors arising from heterogeneous stocks, such as the Jensen and Ehrlich Stamm 11 carcinomata, but also in tumors arising in inbred stocks such as the Japanese waltzing mouse. The behavior of the tumors arising in the F_1 hybrids can not be accounted for on the basis of characters derived either from one of the parents or from both, but only on the basis of the appearance of modifications or new characteristics.

From the evidence in the biological character of tumors of a permanent modification of somatic tissue, it appears logical to regard a tumor as a manifestation of somatic mutation. As a basis for this, there may be modification in the relative value either by loss or addition, or in the nature of factors, any of which, if continuously transmitted thereafter in successive cell generations, will constitute a type of mutation. This, unlike the mutations which may affect the germ plasm, is maintained only through artificial transplantation from one individual to another. The tissue of a new growth has thus in certain respects become foreign to the other tissues. Its growth is no longer controlled by the normal inhibiting influences which constitute a regulating mechanism, but it behaves more or less as a parasite living at the expense of its host; and it may excite a reaction of the surrounding tissue which is in some cases more favorable, in other cases less favorable, to its continued growth. Malignant tumors must have feeble antigenic power as well as sufficient resistance to the normal inhibiting influences to provide for continued growth in the animal in which they originate, otherwise reactions sufficient to destroy them would occur more frequently.

Conclusions.—The results of the experimental investigation of tumors, as well as of clinical and pathological observation, appear to favor the following conception of the nature of tumors and their relationship to the other tissues.

The interreactions of the normal tissues are mutually beneficial so that their relationship is one of symbiosis.

The anomalies and benign growths, while not distinctly harmful, are usually of no benefit to the individual; the relationship is one of commensalism.

The malignant tumors are in many respects parasitic in nature, especially since they develop at the expense of the other tissues of the body. They are so adapted for growth, once they have become established, that they seldom arouse any effective resistance on the part of the body. There is some evidence, however, of a local reaction of tissues unfavorable to the growth of many different types of tumors.

Immunity to transplanted tumor is based on foreignness or incompatibility of tumor and host. This holds true whether the tumor or the animal is taken as the constant factor with which to test the other. Although the degree of foreignness is not sufficient for the production of markedly cytotoxic or cytolytic sera, as when different species are employed, it appears probable that an immune body is formed which, in the presence of the antigen—or living tumor—excites an inflammatory reaction in the tissue around the tumor so that the latter is isolated and eventually destroyed.

Both susceptibility and nonsusceptibility, or the ability to acquire immunity, are inherited, not as a single unit factor but apparently as a complex of mendelizing factors. Nonsusceptibility and susceptibility are apparently based on factor differences, or, in other words, on unlikeness or foreignness. Nonsusceptibility may thus depend with one tumor on a difference with respect to few factors, and with another tumor on a difference with respect to many factors. In the comparison of a stock of Japanese waltzing and several stocks of common mice, the nonsusceptibility of the latter to a carcinoma, J. w. A., is based on a difference with respect to a large number—probably 12 to 14—of independently inherited factors.

Susceptibility is in this material a dominant character, since it is manifested when its factors are present in a single representation, as in the F^1 hybrid. The presence of a single representation of the factors of nonsusceptibility in the F^1 hybrid apparently stimulates the growth of the tumor, for its rate of growth is more rapid than in the Japanese waltzing mouse in which the factors of susceptibility are doubly represented.

There are marked differences in the behavior of various tumors on transplantation in given classes of mice. Even tumors arising in homogeneous races show such differences, and this may be attributed to the acquisition of new characteristics by the soma which are manifested in the development of the tumor. The tumor, since it breeds true with respect to these characteristics in the course of artificial propagation may be regarded as a modification of the somatic tissue which may be termed somatic mutation.

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DESCRIPTION OF PLATE 1.

FIG. 1. Carcinoma (J. w. A.) 98 hours after implantation in a normal control Japanese waltzing mouse (no. 5417). Living tumor is distributed at the periphery, forming a layer with only occasional breaks in its continuity. The necrotic central portion of the implant is free from infiltration.

FIG. 2. Carcinoma (J. w. A.) 98 hours after implantation in a Japanese waltzing mouse (no. 5423) which was injected with immune serum. Living tumor is found in scattered islands and is absent from large portions of the implant's surface. The necrotic interior shows extensive infiltration with polymorphonuclear leucocytes.

CHEMOTHERAPEUTIC EXPERIMENTS ON RAT TUMORS.

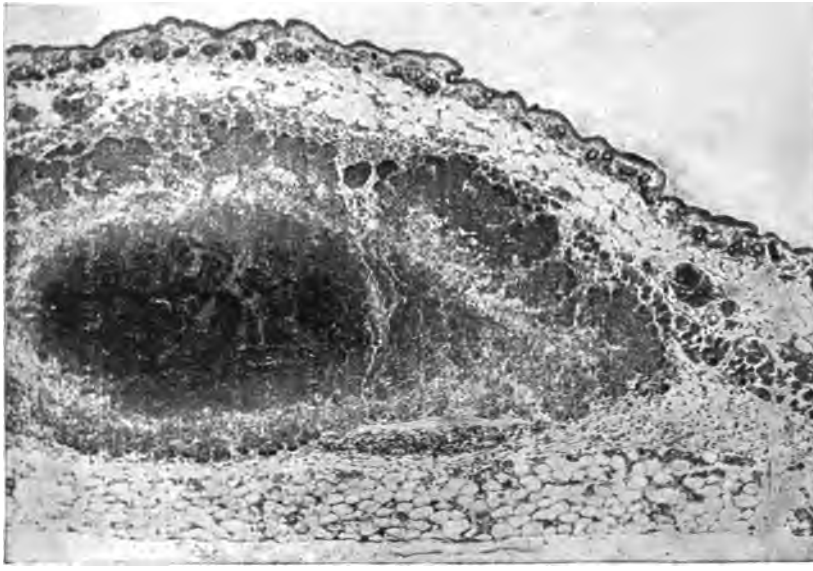
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In discussing a subject of such extent as the chemotherapy of tumors it is quite evident that only isolated features of the problem can be touched on. In the present paper I shall attempt to discuss certain phases of the work which I have been carrying on for several years, in their bearing on the general problem.

1. *The penetrability of the living tumor cells.*—There is at the present time considerable unanimity on the subject of the intravitam staining of cells. Goldmann (3), who was one of the first to study the distribution in the cells and tissues of dyes which were introduced into the circulation, reached certain conclusions which have largely served as the point of departure for subsequent study. He found that certain of the cells took up these dyes, which could then be identified as characteristically colored granules distributed through the cells. Goldmann considered that these granules were preformed elements of cell structure, which had been stained by the dyes. It is possible that this explanation holds true of certain basic dyes (such as janus green, methylene blue, neutral red). Upon this theory it is clear that a staining of granules is simply an alteration of paraplasm, or deuteroplasm, and that, in the absence of a diffuse staining of the cytoplasm we can not speak of a true vital stain of the cells. Indeed, Fischel (2) in Ehrlich's Encyclopädie, holds that there is no such thing as a vital stain in the latter sense.

On the other hand, it is now widely believed that staining of preformed granules is not the correct explanation in the case of the dyes used by Goldmann, which belong almost entirely to the benzidine group. Evans and Schulemann (1) have argued quite convincingly that the presence of the intracellular granules in the cells, in the case of this group of dyes, is due solely to phagocytosis. The cells take the circulating particles of dye out of the circulation, and they then appear as densely stained particles within the cell body. In harmony with this view, it is found that only certain definite types of cells, which act as phagocytes—the "scavenger cells" as Evans calls them, can take up these dyes. The living cells of tumors do not belong



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to this category, hence it is impossible to stain them in vivo with the benzidine dyes. Indeed, I have not been able to stain them with any dyes whatever. The cause of this differentiation between cells is probably biological rather than physical. The scavenger cells are differentiated to pick foreign substances out of the blood for the purpose of elimination. They are, so to speak, a widely disseminated excretory organ. This view is borne out by some instructive experiments carried out by Kite (6). He found that certain dyes (such as azolitmin, congo red, tropeolin 000 No. 1, alizarin sulphonate, indigo-carmin), which fail to penetrate amœba proteus, diffuse freely throughout the organism when injected into it. In other words, the surface of the cell offers an obstacle to its entrance; once in, the color is taken up diffusely by the protoplasm. Again, he states that "if the egg of Asterias be punctured, the acid dyes used penetrate the swollen area for varying depths, but never enter the normal unswollen protoplasm."

Consequently it is found that dead or injured cells behave quite differently toward the benzidine dyes. Their peripheral resistance is gone and they take up the dyes rapidly, presenting a uniform stain. Thus the cells of the kidneys of rabbits treated with sublimate or cantharidin (Gross (4)), and the anterior horn cells in experimental poliomyelitis (MacCurdy and Evans (7)) may be strikingly stained by these dyes.

In this connection the claims of Wassermann and Keysser (10) with reference to the staining of living tumor cells, are worthy of attention. They asserted that the eosin penetrates all the cells of the body, and therefore used it as a carrier ("cytotrochin") for selenium. Their facts, however, do not bear out this assertion. They never succeeded in staining tumors smaller than a cherry pit in size—in other words, tumors in which central necrosis had not occurred. Benign spontaneous tumors, which have no tendency to undergo necrosis, they invariably failed to stain. Internal implantations, which have an infiltrative mode of growth and are well supplied with vessels, Keysser (5) was never able to stain. It seems quite clear, therefore, that they did not succeed, as they thought, in staining the living cells, but only the necrotic areas. In a recent paper (11) I have critically analyzed these results.

2. *Staining of necrotic areas.*—Inasmuch, therefore, as the conditions do not permit of staining the living cells of the tumor, one is perforce driven to a study of the staining reactions of the necrotic parts of tumors. It is this phase of the problem to which I have chiefly devoted my attention. The literature which bears on the subject is to be found almost exclusively in the remarkable series of studies which have been published in the last few years from the Sprague Memorial Institute (8) under the direction of H. G. Wells, dealing very largely with the staining reactions of tuberculous tissue.

The first question which was studied in my work concerns the distribution of crystalline substances in necrotic tumors, as compared with the normal tissues of the body. Rats bearing necrotic tumors received intravenous or subcutaneous injections of solutions of sodium iodide. After varying intervals of time the animals were killed, and the various tissues of the body were analyzed for their iodine content. The chemical work was carried on by Dr. Van Alstyne, to whom my thanks are due. It was found that the blood regularly contained the largest proportion, and after this came the tumors and the liver. The other tissues, except the kidney, have regularly shown very much less iodine. If the tumor was small and nonnecrotic, its proportion of iodine was very small. These findings are entirely in harmony with those recently published by Wells, DeWitt, and Corper (12) on the distribution of potassium iodide in tuberculous tissue. They interpret their results as indicating that "the large amount of iodine present in necrotic tissues, whether tuberculous or otherwise, is dependent on purely physical conditions—i. e., the destruction of the semipenetrability of the cells."

3. *Localization of dyes in tumors.*—The relation of the dyes to the necrotic tissues of tumors is of considerable interest. Wells, DeWitt, and Corper arrived at the conclu-

sion that "necrotic tissues, whether tubercles or other lesions, behave like any non-living colloidal mass into and from which crystalloids diffuse readily and rapidly, while colloids enter very slowly or not at all." In support of this view they showed, by a very ingenious application of anaphylactic methods, that egg white does not penetrate the caseous tubercle. However, their theory does not appear to take account of all the facts. Thus Dr. DeWitt (13) herself has shown in another paper that caseous tubercles can be thoroughly penetrated and stained by trypan red and by trypan blue. Both of these dyes, however, are colloidal. As an actual fact, the relationship between foreign colloids in the circulation and necrotic tissues are very much more complex than might be inferred from the hypothesis above outlined. In illustration of this fact I might instance the following observation:

During the period in which I was studying the distribution of dyes in tumors the rats in our laboratory fell a prey to a very serious epidemic. The disease manifested itself as a progressive caseating inflammation of the lungs. Macrosopically and microscopically the lesions presented a striking resemblance to human phthisis, without, however, showing cavity formation. Very frequently I autopsied animals in which not only necrotic tumor tissue but also these caseous areas in the lungs were present. If such animals had previously been injected intravenously with appropriate dyes of the benzidine series, it was almost invariably possible to make a very striking observation. The dyestuff (e. g., congo red) regularly produced intense discoloration of the necrotic tissue in the tumors, but in no instance, over dozens of observations, did it produce the slightest staining of the caseous areas in the lungs. Congo red, it may be added, is a highly colloidal dye. This statement is based on the fact that the dye does not diffuse through membranes. Certain other properties of its solutions seem, however, to range it among the highly dissociated electrolytes. Such, for instance, are the effects upon the boiling and freezing points, and the fact that its solutions are optically clear. Therefore one may conclude that the relation of colloids, or of colloidal dyes at least, to necrotic tissues is not uniform.

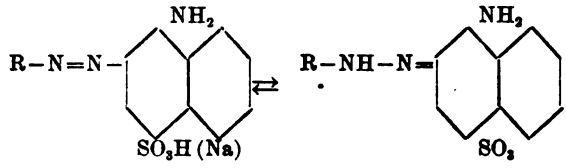
As a matter of fact, the diffusibility of dyes into a colloidal mass depends upon a variety of circumstances. As regards the dye, not only its degree of diffusibility through animal membranes which determines its value as a colloid, but its electrical charge, its chemical reaction, and its chemical composition all play a rôle. As regards the colloidal mass again, its physical composition is of importance, as is also its electrical charge and its chemical composition. A knowledge of these factors permits of a fair guess, but no more, as to the result. Thus Teague and Buxton (9) found that agar, which is supposed to carry a negative charge, was easily penetrated by acid dyes, anilin blue diffusing as actively as the much more slightly colloidal eosin. Of the basic dyes, only the slightly colloidal ones diffused in any amount. Even moderately colloidal basic dyes showed little capacity to invade the agar. The basic dyes, however, stain the agar intensely, whereas the acid dyes leave it uncolored. Congo red and azo blue constitute an exception to the latter rule, and although they are acid dyes, diffuse only slightly but stain intensely. Thus it will be seen that no generally valid law for the diffusion of all colloids, or colloidal dyes, into necrotit tissues can be formulated. The same dye may react quite differently to differenc types of necrosis even in the same individual.

4. *Localization of the benzidine dyes.*—Of the benzidine group, a considerable number of dyes have been tested, starting with congo red. In all over 20 dyes have been included in the present study, all of which are well-known chemical individuals of the benzidine group, representing substitutions either in the benzene or in the naphthalene nucleus by sulphuric acid, hydroxyl, methyl, salicylic acid, and other groups. In general these dyes tend to localize first in the peripheral zone of the central necrotic area. If repeated injections are made, they gradually penetrate the entire necrotic mass. Eventually, with the use of very large amounts, some of these dyes may

slightly discolor even the healthy, actively growing rim of tumor tissue, owing to the presence therein of minute foci of necrosis. For the other tissues of the body the stains have a varying degree of affinity, depending on the degree to which they are taken up by the scavenger cells. Superficially it would appear that certain dyes have a relatively specific tropism, if one may use this term, for the necrotic areas of the tumor. It is, however, not safe to judge of the localization of the dyes by the discoloration of the skin. Animals which have been treated by intravenous injections may on autopsy present no apparent evidence of discoloration, either in the skin or in the internal tissues. If, however, the liver be boiled for a few minutes—a procedure long ago suggested by Ehrlich—the masked discoloration at once becomes evident. Observing this precaution, I have never yet found discoloration in the tumor which was not accompanied by some discoloration in the liver, either alone or with other of the parenchymatous viscera. On the other hand, many of the dyes appear to lodge in far greater amount in the necrotic area of the tumor than in any other tissue, and also to remain there for a longer period. Whether they are actually present in greater amount there than in the liver is, however, very doubtful, owing to the fact that the underlying colors make an ocular comparison extremely fallacious. In some experiments, equal weights of liver and of necrotic tissues were suspended in equal volumes of water, and the colors of the resulting solutions were compared. It did not appear that the liver contained less than the tumors in any instance; indeed, it occasionally contained more. Thus, it is probably correct to say that none of the benzidine dyes manifests more than a relative specificity for the necrotic tumors. And it is not unlikely that even this apparent specificity is actually nothing more than the expression of a retarded rate of absorption from these poorly vascularized areas. It is interesting to note that these dyes manifest the same predilection for the necrotic areas of human tumors. A solution of congo red was injected intravenously into a patient with cancer of the breast in the hope of helping in the detection of the carcinomatous areas at the subsequent operation. When the breast, with the axillary contents, was removed, it was found that the necrotic areas of the tumor foci, both in the breast and in the axillary nodes, were stained an intense red. The living areas of tumor tissue, as well as the normal tissues of the breast, appeared to have their normal coloration. It seems unlikely, however, that this method will ever prove of any clinical value.

5. *Metachromasia.*—An interesting phenomenon is the changes of color undergone by some dyes after they enter the necrotic areas. This color change has been described as metachromasia, adopting the terminology of pathologists. The cause of the phenomenon is somewhat obscure. It is, of course, well known that some of the benzidine dyes are markedly affected in color by the mineral acids. Indeed, congo red has on this account been adopted as an acid indicator. But the organic acids have this effect only in high concentration and in minor degree. Moreover, the color changes are not similar to those induced by mineral acids, but resemble more the changes induced by the localization of dyes in amyloid. In seeking to determine the cause of these changes I was led to test the effect of solutions of various polypeptids on the benzidine dyes. I found that they effect changes quite similar to those produced in vivo by the necrotic tissues. Thus, if solutions of congo red be mixed with solutions of various amino-acids, a series of changes in color can be produced, slight, for example, in the case of glycyl-glycine, more marked with leucyl-asparagine and alanyl-glycine, and pronounced in the case of glycyl-glycyl-leucine. The color does not change to blue, as it does with mineral acids, but rather to a deep mahogany brown. Mr. Carruth has suggested to me that color-changes in dyes like congo are to be explained by a separation of the base (Na) from the acid radical, which make it possible for the dye to assume the isomeric quinone form. Although the free congo acid may exist in a red form (azoid), this form is not stable in aqueous solutions and passes

instantaneously into the blue form (quinoneimide). Intermediate shades—brown violet, etc.—must represent the presence of certain amounts of each form:



At all events, it appears that the chemical conditions present in the necrotic tissues results in the production of some change in the character of the dye compound. In the same animal the normal tissues, such as the skin, which take up the dye, present it in an unaltered form. This fact led to the hope that the necrotic areas might conceivably be competent to break up compounds of these dyes with toxic substances, freeing the latter for attack upon the surrounding healthy tumor cells.

6. *Therapeutic effects of certain compounds.*—The method of study followed in determining the effect of the dyes upon tumor growth and a typical result are illustrated by the following protocol. In this case the dye used was Columbia violet R, supplied by the Berlin Aniline Works. It is a diphenyl-disazodi-amino-naphthol-sulphonic acid.

A rat, series A, X, weighing 170 grams, has a sarcoma, the Buffalo strain, inoculated 27 days previously, now measuring ½ by 1¼ inches, firm, not ulcerated.

April 24, subcutaneous injection: 3 cc. 0.5 per cent C. v. R. No constitutional effects; no discoloration except at site of injection.

April 25, the same dose.

April 26, the same dose.

April 27, no general discoloration. Exploratory section of tumor: center necrotic, peripheral necrotic rim shows a violet discoloration. Two pieces removed from healthy margin and planted in 10 rats, in all of which "takes" occurred. Skin sewed up and soon healed.

May 11, 1½ cc. 1 per cent C. v. R., intravenously. Tumor has grown to 1 by 2½ inches.

May 13 and 14, 2 cc. 1 per cent, intravenously.

May 17, animal died.

Autopsy: Tumor unstained in growing margin. Necrotic core shows all transitions in color from salmon yellow at center to violet at margin. Infiltration of lungs, with severe caseation. No discoloration. Liver and kidney on boiling show slight discoloration.

A series of compounds analogous to congo red were made for me by Mr. Carruth, working under Prof. Orndorff in Ithaca. In determining the compound to be made we were perforce guided by largely speculative considerations as to their probable effects upon the living cells. Unfortunately the data upon which such calculations can be based are few and inadequate. Aside from this consideration, however, it is evident that chemotherapeutic compounds, to be of any possible service in the treatment of tumors, must possess certain other properties. They should not be highly toxic to the organism. They must, of course, be soluble. They should be fairly stable in solution, yet should be dissociable in the necrotic areas of the tumors. These properties are not such as can be foretold of any given compound with certainty, hence the investigation resolved itself into an empirical study of such of the compounds as seemed most favorable.

The compounds which were tested out on the rat tumors are comprised in the following list:

In solution.

1. Ortho-diselenide dye.
2. Congo-formaldehyde compound. No free formaldehyde present. Ten grams congo red per liter; 0.43 grams of formaldehyde per liter.
3. P′-arseno-aniline dye, 1 per cent.
4. Mercury congo blue, 0.5 per cent; probably a mercuramino compound.

In powder form.

5. Recrystallized congo red.
6. Recrystallized bordeau extra.
7. Barium salt of congo red.
8. Potassium salt of congo red.
9. Zinc salt of congo red.
10. Copper salt of congo red.
11. Copper salt of bordeau extra.
12. Congo di-triazine.
13. Benzidine < Sulphanilic acid. / Beta-naphthol.
14. Thio-aniline dye.
15. Benzidine < Atoxyl. / Beta-naphthol.
16. Benzidine < Atoxyl. / Naphthionic acid.
17. Soluble selenium congo red.
18. Salmon red, thiazol derivative.

The exact composition and probable formulæ of these compounds will not be here discussed. Consideration of solubility, toxicity, and other properties will also be deferred to a future publication. The present paper is concerned only with the analysis of their therapeutic effectiveness.

All the compounds appeared, judging by the gross discoloration of the tissues, to localize electively in the necrotic areas of the tumors. All the injected animals in which tests were made, however, showed discoloration of the boiled livers. The localization was further controlled by chemical analysis of the organs which, at least in the case of the arsenic compound, could be considered to give reasonably accurate results. The maximum yield of arsenic per gram of substance was obtained from the liver, while the tumor and the kidney came next. The arsenic content of the other organs and tissues was low. From these results it would appear that localization in the tumors was only relatively specific. It is, however, possible that the arsenic reached the liver only after the compound had been dissociated in the necrotic areas of the tumors.

In judging of therapeutic effects, three criteria were employed, namely, the rate of growth of the tumors, their transplantability, and the number of retrogressions. The details of the method have already been illustrated. None of these three criteria has an absolute value in the type of tumor which formed the basis of this study, inasmuch as they all vary to a remarkable degree. At times the tumor "takes" in a large percentage of the inoculations, while at other times, for no ascertainable reason, this percentage is greatly reduced. The rate of growth and the percentage of retrogressions also vary strikingly in different generations of the tumor. For this reason it is always necessary to plant a considerable series, of which at least half are kept as controls, while the remainder are reserved for the purposes of the experiment. The conditions are unfortunately such as to preclude the determination of small effects; on the other hand a definite and considerable influence on the life history of the tumors could certainly not escape detection. Judged by these standards, the results obtained were not encouraging. In only three out of the entire list—namely, numbers 3, 4, and 14—were any effects ascertained, and these three proved so highly toxic to the rats when given in therapeutic amounts that it seemed questionable whether the effects on the tumors were attributable to the specific action of the drug or to the general effect upon the health of the animal. At all events, none of the substances possessed that combination of properties which would make them available for the effective treatment of the rat tumor. The principal object of the investigation, therefore, failed to be accomplished.

I wish to acknowledge the constant help and advice of Prof. Orndorff and of Mr. F. E. Carruth, without which this work would have been impossible.

CONCLUSIONS.

1. Living tumor cells are not penetrated by colloidal dyes.

2. The necrotic areas of tumors contain a larger amount of iodine than do the other tissues of the body after the intravenous injection of sodium iodide.

3. The necrotic areas of tumors present an intense discoloration after the intravenous or subcutaneous administration of dyes of the disazo group.

4. The discoloration of these tumor areas is very frequently associated with some discoloration of the liver, while the other tissues of the body remain macroscopically unstained.

5. The staining of the necrotic areas of tumors is not due solely to the death of the cells, inasmuch as areas of pulmonary caseation in the same rats do not present any discoloration.

6. The localization of colloidal dyes in necrotic tissues is not a simple physical phenomenon, subject to the laws of diffusion of fluids into nonliving-colloidal material. The diffusibility of the dyes through membranes, as also the electrical charge, the chemical reaction, and the chemical composition of both colloids influence the result.

7. A peculiar alteration in the color of dyes of the benzidine group occurs in necrotic areas. This has been described as metachromasia.

8. A series of new synthetic compounds analogous to congo red were injected into tumor-bearing rats. No definite therapeutic effect could be determined.

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THE APPLICATION OF CHEMICAL METHODS TO THE STUDY OF CANCER.

By CASIMIR FUNK.

The aim of the author in presenting this paper is to indicate the chief lines of biochemical research for the study of cancer and to discuss the results obtained. This branch of chemistry dates only 10 or 15 years back and the results so far obtained are only the first attempts to throw light on the etiology of tumors from chemical point of view. The reason why so few results were obtained can be very likely explained by the fact that so long as Cohnheim's theory was accepted for the explanation of the tumor etiology, there has been very little scope for the application of chemistry to this branch of medicine. This theory explained the origin of tumors by the preexistence in the adults of embryonic cells which had the power to resume unlimited

growth as the result of injury or irritation. At the present time this and other theories based more or less on the vitalistic conception of cell energy have found a serious rival in the parasitic theory and recently in the chemical theory of cancer. As the hypothetical parasite, however, must stimulate cells by chemical means, as a simple presence of a parasite could not explain the sudden multiplication of cells, both heories need for their final deductions of serious chemical studies.

THE DETERMINATION OF VARIOUS SUBSTANCES IN THE TUMORS.

The analyses were carried out usually in this way that the amount of the different tumor constituents was compared with this of the tissue where the tumor originated. Here the question arises whether it is correct to compare, for instance, a sarcoma of the breast with the tissues of the normal breast, which no doubt must be chemically different from another, and this diminishes the ultimate value of such determinations. More promising would be to hunt for substances which are only present in tumors and not in normal tissues. As these investigations are the only ones which give us an idea on the nature of chemical processes going on in tumor cells, their results may be shortly recorded.

THE INORGANIC CONSTITUENTS.

Beebe studied the relationship between sodium and potassium to calcium, which he found larger in quickly growing tumors; in young tumors only potassium was found and no calcium; this work was confirmed by Clowes and Frisbie. Medigreceanu investigated the quantity of manganese in experimental tumors.

THE ORGANIC CONSTITUENTS.

Proteins.—Petry determined the amount of nucleo-albumins in tumors and he found in a breast carcinoma this latter protein making 50 per cent of the total protein, whereas in the normal breast it is only 30 per cent. Beebe found a nucleohistone in metastases of a carcinoma of the breast, but none in the primary tumor, which indicates a chemical difference between these two tissues. Wolff and Blumenthal have recorded an increase of albumen in tumors at the expense of globulin. Wolff has isolated from ascites fluid of a cancer patient a protein giving on hydrolysis 35 per cent of glutamic acid.

Aminoacids.—Bergell and Dörpinghaus have hydrolysed tumor proteins and have found an increase of glutamic acid, alanine, phenylalanine, aspartic acid, but espepecially of diamonacids, this latter fact being recently confirmed by Kocher. On the contrary, Neuberg did not find any differences between the metastases of a carcinoma of the stomach as compared with the somatic tissue. Abderhalden and Medigreceanu have analyzed a carcinoma of a cow's liver, a rat sarcoma, and a mouse carcinoma on their content of tyrosine, glutamic acid, and glycine, and have obtained nearly identical results. Fasal has determined tryptophane in several tumors and Eppinger the same aminoacid in a melanosarcoma.

OTHER CONSTITUENTS.

Beebe and Schaffer have found an increased amount of pentose in a breast carcinoma. Wolter found the phosphatide content of the liver tumors diminished and the protein phosphorus increased.

No attention so far was paid to protein-free filtrates from the tumor extracts—a problem, as we will see later, of particular interest. This research is now proceeding in the laboratory of the author, the spindle cell and the osteo-chondro-sarcoma of the fowl being compared with the normal muscle of the same animal.

FERMENTS IN CANCER.

This study was initiated by Blumenthal and Wolff and continued by Bergell and Dörpinghaus and also by Neuberg, these authors have found that the tumors are more

resistant to pepsin than normal tissues. This resistance is destroyed by heat and is not due to antiferments. An increased autolysis in tumors was first described by Petry; the tumor extracts were not only found to break down proteins, but also albumoses, into simple aminoacids. Following Blumenthal and Wolff the addition of tumor extracts is able to activate also the autolysis of other tissues. Abderhalden and his collaborators (Medigreceanu and Koelker) have investigated the behavior of tumor extracts toward certain polypeptides and peptones by means of the optical method. In summarizing the results of these extensive studies we may state that no marked difference so far was observed between normal tissues and tumors as regards their action on polypeptides, but a difference was noticed by using silk peptone. Serum of dogs with Sticker's tumor showed the presence of peptolytic ferment in difference to normal dog serum. Abderhalden and Pincussohn by using d-Alanyl-glycyl-glycine made the observation that normal tissue splits off alanine first from this tripeptide whereas the tumor extracts separate glycine first. These studies were also applied for the diagnosis of tumors.

SERUM DIAGNOSIS OF TUMORS.

The most important methods used are the dialysis and optical methods of Abderhalden, the reaction of Freund-Kaminer, the meiostagmin reaction of Ascoli, and the complement deviation method of v. Dungern. The reaction of Abderhalden is based on the alleged property of the organism to destroy substances foreign to them which appear in the blood. Assuming for the present that the theoretical basis of these studies is correct, which is not certain, the results obtained by most of the workers, including the author, were not satisfactory. By using the micro Kjeldahl or the micro van Slyke method no increase of amino-nitrogen was obtained by action of the tumor serum on tumor substrates; the same negative results were obtained with the optical method. The reaction of Freund-Kaminer is based on the assumption that normal serum is able to destroy cancer cells—a property lacking in tumor serum. The meiostagmin reaction observes the diminution of viscosity of tumor sera under the influence of certain fatty acids. This method was extensively tried by the author, and by using cod liver oil instead of fatty acids slightly better but still unsatisfactory results were obtained. As the v. Dungern's method also met with much criticism, we can say that at present we do not possess a single method for a successful diagnosis of tumors. It seems that the most promising way would be an intimate knowledge of the chemical constituents of normal and tumor sera. By analyzing the sera of chicken with sarcoma, I was able to demonstrate a very marked diminution of nitrogen in the serum, with a tendency of this difference increasing with the time elapsed since inoculation. It is therefore probable that the diagnosis of tumors will shift from unknown factors to a determination of chemical constituents easily recognizable and easily tested.

CHEMOTHERAPEUTICS OF CANCER.

The infectious nature of the tumors being uncertain, the chemotherapeutical treatment of cancer does not appear to be promising. Positive results so far obtained with colloidal metals, selenium and tellurium compounds, and arsenic were all obtained with rats and mice and failed when applied to man. The cause of this failure is that these tumors, which show very often spontaneous absorption, are not well adapted for these studies. Chicken tumors seem to be more suitable for these experiments; so, for instance, a number of arsenic compounds were tried by the author on chicken sarcoma, with no visible effect.

INFLUENCE OF DIET ON THE GROWTH OF TUMORS.

We are able to influence the growth of tumors by using a diet either insufficient in quantity or in quality. Such experiments were performed by Cramer and Pringle and Rous. Sweet, Corson-White and Saxon, Hopkins, and the author have used for

this purpose a diet lacking in vitamines, and have observed a very marked inhibition of tumor growth. As apparently the affinity of the tumor cells to the substance necessary for growth is greater than the affinity of the somatic cells, no complete inhibition of tumor growth could be obtained by this method. Similar experiments were performed by Beebe and van Alstyne on the influence of the addition of lactose to a casein and lard diet. Nothing could better demonstrate the influence of diet on tumors than the experiments of the author on the successful transplantation of foreign tumors by feeding the animals on the tumor used for inoculation.

GROWTH OF TUMORS AND THE BODY.

The results of Osborne and Mendel, Hopkins and McCollom, and Davis have demonstrated the fact that young animals require for their growth process a special substance, which in the light of the results of Casimir Funk and Macallum, seems to belong to the class of vitamines. For these experiments yeast has proved to be an excellent starting material, and a chemical fractionation will show whether the growth of the body and of the tumors requires the same or different substances.

ETIOLOGY OF TUMORS.

The discovery by Rous of tumors in chicken, which are transplantable by means of cell-free filtrates, opens a new possibility, namely, that they are propagated by an unstable chemical substance. The causative agent is so highly unstable that heating over 50°, and even drying in vacuum, will destroy it. As a preliminary experiment toward the elucidation of the etiology of these interesting tumors, it was tried to transplant the spindle cell sarcoma by means of an alcoholic extract of this tumor, and on several occasions a positive result was obtained. In fact, it is quite conceivable that tumors are produced by a chemical substance in a similar way like the orientation of the tissues in an embryo and the growth of animals are directed in a chemical way. Cancer is possibly a metabolism disease, in which the metabolism of the growth promoting substance is affected. The age at which the tumors usually appear supports this view.

All the problems recorded in this paper render the collaboration of the physiological chemist toward the elucidation of the etiology of cancer highly desirable. The pathological research in cancer, so successfully started by Jensen, Ehrlich, Bashford, and others, gave us an enormous amount of valuable data, but it appears doubtful whether the pathological line alone will solve the cancer problem. The necessity of a new chemical technique and extensive facilities calls for establishment of special research places for the chemical study of cancer which would supplement the studies of pathologists in this direction.

The CHAIRMAN. We will now proceed with the discussion of the general subject of the evening.

Dr. WOGLOM. I think that Miss Slye is to be heartily congratulated on having so fully confirmed the findings of Tyzzer in our country and of Murray in London. Murray has been publishing work along this line for the last 10 years. His last paper, I think, came out two or three years ago. Murray finds that in lines of cancerous ancestry there is an incidence of something like 15 per cent of mammary cancers in mice that live to be more than a year and a half old. In the control mice, on the contrary, there is about 8 per cent of mammary cancer. The control mice are those that lost neither a grandmother nor a mother from mammary cancer. Now, Murray, being a cautious man, submitted his figures to an expert

statistician who found that the chances were three to one in favor of Murray's results being correct. It seems to me that Miss Slye has here invaluable material and that these results ought to be analyzed by a statistician in exactly the same way that Murray's work was analyzed, in order that we may have some basis of comparison between the two stocks of mice. In the meantime I think some protest should be made against including the lung tumors of mice with tumors which are undoubtedly cancerous. I do not think any of us feel sure that these lung tumors are really carcinomata. Perhaps Dr. Tyzzer has seen more of them than any of us and he possibly will express an opinion on this. I do not think people are so sure about it. Then, in the second place, I do not think it is wise to count a mouse as cancerous that dies before it develops a cancer; to count that mouse as cancerous because his descendants developed cancer. I do not speak as a biologist nor as a statistician. I speak as a pathologist. I think only a board of statisticians, biologists, and pathologists could decide on the justice of such a course.

Dr. TYZZER. I would like to make a few comments on the inheritance of spontaneous tumors. There are certain well-known Mendelian factors which are concerned in the production of tumors. I refer to the inheritance of sex. Sex is a perfectly well-known inherited factor. The sex factor may act in two ways. The two sex factors may act in the following manner: In a restrictive manner with respect to certain tumors—that is, they are sex limited. For example, the ovarian tumor is limited to the female; the testicular tumor, to the male. Then there is the liberative action of these factors. We have in mice, probably more than in human beings, the mammary tumors, restricted to the female; it is rather rare to get a mammary tumor in the male mouse. There is something in the development of the female sexual organs which in a way is liberative, so that in the development of the mammary gland we get more tumors of the mammary gland in the female. I do not believe that the development of tumors can be shown to be based on any single factor. There must be multiple factors present in the development of spontaneous tumors, just as in the development of the inheritance of susceptibility. The pathologist will say that environment is the essential factor, but I would like to point out here that environment of the cells is to a large extent inherited. The environment of the female mammary gland is to a large extent subjected to internal secretions which are not found in the male.

The CHAIRMAN. Dr. Loeb, will you be kind enough to close the discussion?

Dr. LEO LOEB. Dr. Woglom's remarks in regard to Dr. Slye's experiments concern my own experience just as well as that of Dr. Slye, so I might perhaps answer Dr. Woglom. Dr. Murray's

experience, I think, does not hold good on the strict basis of the ordinary scientific work in heredity. Murray found differences between 8 and 18 per cent, if I remember correctly, for he had two strains of mice. He selected mice whose ancestry had tumors, cancers, and those whose direct ancestry did not have cancer; but those whose direct ancestry did not have cancer had cancer somewhat further back. Now, if we take a strain very poor in tumors and select as ancestors a mother who had accidental tumors, and take another strain very rich in tumors and select as ancestor a mother who accidentally did not have tumors, then we should, according to Murray's procedure and method, find, if we persisted, that mice from a strain rich in tumors had less tumors than mice from a strain poor in tumors. If the method gives correct results these results can only be accidental—at best, probably three to one; but that is not an actual scientific result.

On the other hand, if we proceed as Dr. Slye and myself have done for quite a large number of years, and breed a large number of generations, have thousands of mice carefully recorded, and find that in one strain there is always present 70 to 80 per cent of tumors in various generations, and that in another strain, maybe absolutely under the same conditions, only 2 to 3 per cent show tumors, it is absolutely impossible that any objection can be made to concluding that there is hereditary condition since the environmental condition is absolutely the same. On the other hand, I think Murray's experiments are very open to criticism.

Tyzzer is the first one who really tried to carry out experiments in heredity on a large basis, but he used the same method which Murray used, and therefore his experiments could not give definite results. I want to say a few words concerning Dr. Tyzzer's experiments in regard to serum in cancer. I find these exceedingly interesting. These experiments which Dr. Tyzzer reported to-night seem to prove that the combination of serum with the tumor cells actually causes a metabolic product to be produced by the cancer cells which causes a contraction of the lymphocytes. There are the same conditions which are found in normal tissues; and on the basis of a large number of experiments I came to the same conclusion with respect to normal tissues and suggested that in the case of tumor tissues the same thing would hold true. Dr. Tyzzer's experiments provided experimental proof for these suggestions.

Dr. HOFFMAN. At a meeting of the statistical committee of the American Society for the Control of Cancer and of the statistical revising board of that committee a number of matters were discussed more or less pertinent to the discussion of this evening. As Dr. Woglom has pointed out, a considerable amount of statistical aid might possibly be rendered to Miss Maud Slye in her very admirabel

work, and I desire to assure her on behalf of the committee that they are most willing to aid her in any way to make the interpretation of her data in so far as they are purely statistical. No one who has had much experience with statistical work fails to realize the enormous number of pitfalls, the ever-present liability to error arising not only from the inadequacy or the limitation of the facts, but partly because of bias, partly because of the inadequacy of our judgment, and largely because of faulty methods of statistical analysis. The resolution which the committee adopted and which they would like to have this section adopt in behalf of Section VIII of the Second Pan American Scientific Congress, reads as follows:

Whereas cancer is one of the leading causes of death in adult life throughout the Western Hemisphere; and

Whereas the mortality from cancer in the principal countries and cities of the Pan American Union is actually and relatively on the increase; and

Whereas the statistical study of cancer is of great practical importance to the cause of cancer research in all its scientific aspects; be it

Resolved by the Second Pan American Scientific Congress, That they most respectfully and urgently suggest to all the Governments of the Pan American Union that they adopt without needless delay uniform methods of cancer classification and statistical tabulation with a due regard to the age, sex, and race of the deceased, of the organs and parts of the body affected by malignant disease, in conformity to the principles of the Bertillon international classification of the causes of death as employed and standardized by the Division of Vital Statistics of the United States Census.

I move the adoption of the resolution.

The CHAIRMAN. You have heard the resolution. What is the pleasure of the section in regard to the disposition of this resolution?

Dr. WHITMORE. I move it take the usual course.

Seconded and approved.

The CHAIRMAN. The following papers will be read by title:

Linfocitosis sanguínea en los sifilíticos, by Cándido Patiño Mayer and Augusto Celestino Gourdy.

Granuloma venéreo, by Federico Susviela Guarch.

LINFOCITOSIS SANGUÍNEA EN LOS SIFILÍTICOS (SIGNO DIAGNÓSTICO Y PRONÓSTICO).

Por CÁNDIDO PATIÑO MAYER Y AUGUSTO CELESTINO GOURDY,

Buenos Aires, Argentina.

HISTORIA.

La sífilis es, sin duda, una de las enfermedades infecciosas más esparcidas y la que cuenta por consiguiente con uno de los porcentajes más subidos de enfermos; nada extraño tiene, pues, que haya merecido la atención de muchos observadores de varias generaciones; pero su conocimiento más profundo y sus mejores adelantos, no se alcanzaron tanto en los largos años transcurridos, como en los pocos que pasan desde el momento en que se descubre el espiroquete pálido por Schaudinn y Hoffman en 1905.

Justo es que hasta entonces, una enfermedad tan difundida, fuera objeto de consideraciones más que todo de orden esencialmente clínico y que a partir de ese momento recibiera una atención más fundamental y científica por la contribución del laboratorio.

El período experimental iniciado, algo antes, por Nicolle y Hamonic y continuado por Metchnikoff, Roux, Bertarelli, etc., señala una nueva era caracterizada por dos órdenes de hechos: el diagnóstico y el tratamiento del lues. Este último recibe un gran impulso con los compuestos arsenicales de Ehrlich que permiten intentar la esterilización de la sífilis mediante el tratamiento abortivo.

DIAGNÓSTICO.

El diagnóstico, merece también una especial atención, y es así como se descubren una serie de procedimientos biológicos que tienden a ese objeto:

(*a*) Comprobación de la existencia del treponema en el chancro.

(*b*) Intradermo y cuti-reacción con la sifilina de Nicolas, Fabre, Gautier y Charlet.

(*c*) La suero-reacción de Wassermann (principalmente de la sangre y del líquido céfalo-raquídeo).

(*d*) La luetina-reacción de Noguchi.

(*e*) El estudio del líquido céfalo-raquídeo: examen citológico, químico y biológico.

(*f*) La reacción de Nonne y Apelt.

(*g*) La reacción de Landau.

(*h*) La coagulo-reacción de L. Hirschfeld y R. Klinger.

Estos son los procedimientos que hasta nuestro estudio han sido señalados para poder diagnosticar la sífilis.

NUEVO SIGNO.

Con nuestro trabajo hemos querido agregar un nuevo signo: el de la linfocitosis sanguínea, que, descuidado por los observadores, ha merecido de nuestra parte un estudio especial, dándole todo el valor que debe tener no sólo en el diagnóstico, sino también en el pronóstico del lues.

Ya el Dr. Gourdy en su tesis sobre la suero-reacción de Wassermann tuvo oportunidad de referirse a la linfocitosis de la sangre de los luéticos, y ahora nosotros al estudiar detenidamente el punto, lo hacemos con un criterio más amplio, llegando también a conclusiones nuevas e interesantes.

LINFOCITOSIS SANGUÍNEA.

Entendemos por Linfocitosis sanguínea, la proporción de linfocitos, por ciento, superior á la cifra normal. Esta linfocitosis normal según los diversos autores oscila entre 20 por ciento y 25 por ciento y hasta 28 por ciento para Jolly, excepción hecha del niño de primera infancia, en el cual la proporción normal es mucho mayor, pudiendo llegar hasta 70 por ciento y que, como se comprende, no ha sido considerado en este trabajo.

Ahora bien; esta linfocitosis normal se halla aumentada en los sifilíticos y es esa linfocitosis patológica sifilítica, la que nosotros pretendemos hacer valer en la sífilis como signo de diagnóstico y aún de pronóstico.

SIGNO PATOGNOMÓNICO.

Sería quererse encerrar dentro de límites muy estrechos y alejarse así del criterio clínico, el pretender pensar que la linfocitosis es únicamente patrimonio del lues, como sería absurdo sostener que por el hecho de pertenecer a un grupo de enfermedades no puede tener valor diagnóstico en la sífilis.

El signo patognomónico no pertenece ni a la clínica ni al laboratorio; hasta un mismo germen puede producir por su localización diferente, por su virulencia, por las asociaciones, procesos anatómicos diversos. También quisiéramos recordar en este

momento que la suero-reacción de Wassermann, de valor inestimable en el diagnóstico, pertenece a un cierto grupo de enfermedades, como la frambuesia, fiebre recurrente, lepra, saturnismo, psoriasis, lupus eritematoso, algunos palúdicos, escarlatinosos, y estados caquéticos; a veces en periodos post-clorofórmicos, peste, beriberi, en los tripanosomiásicos y colesterinémicos; algunos han pretendido hallarle en sujetos normales. Sin embargo, ¿quien se atrevería a restarle su inmenso valor en el diagnóstico de la sífilis?

LA LINFOCITOSIS SANGUÍNEA EN OTRAS ENFERMEDADES.

Estos comentarios nos los sugieren la presencia de la linfocitosis en otros procesos no sifilíticos: así por ejemplo, se le encuentra en un porcentaje subido en el paludismo, como el Dr. Patiño Mayer, entre otros, lo ha hecho notar, estableciendo la linfocitosis palúdica transitoria y la permanente; se la halla también en estados escrofulosos con hipertrofía de los ganglios y de las amigdalas; en la persistencia del timo y en el bocio exoftálmico; en la diabetes; en la obesidad; en el mixedema y estados hipotiroideos; en la acromegalia; en algunos neurópatas; en la tuberculosis; en algunos procesos crónicos y enfermedades de la sangre; en la tripanosomiasis y leishmaniosis.

Como acabamos de ver, la linfocitosis sanguínea se halla en un cierto grupo de enfermedades, pero esto, como se comprende, no le quita importancia en el diagnóstico del lues; fácil será establecer el distingo por los caracteres clínicos y los datos hematológicos en cada caso.

SÍFILIS.

Por otra parte la linfocitosis sanguínea del sifilítico es generalmente elevada, pudiendo llegar en ocasiones hasta 70 y 80 por ciento. Dentro de la fórmula citológica, se presenta bien característica, la linfocitosis elevada, acompañándole una cifra normal de leucocitos y de hematíes (estos pueden estar disminuídos en las graves infecciones). La linfocitosis sanguínea tendría, pues, según nuestra manera de ver, una gran importancia en la sífilis, importancia que no ha llamado la atención hasta el presente a los sifilógrafos, ni a los dedicados al estudio de la hematología, sin embargo, dada nuestra larga observación, de varios años a esta parte, y que comprende más de 500[1] observaciones de distintos períodos del lues, nos creemos autorizados para darle toda la importancia que merece como contribución a su diagnóstico y aún a su pronóstico.

INFECCIONES ACCIDENTALES.

Debemos, no obstante, llamar la atención sobre algunos resultados de exámenes de sangre, en aparente contradicción con la fórmula general propia del sifilítico, donde se ve una leucocitosis con predominio de los polinucleares neutrófilos; se trata aquí, de infecciones accidentales, concomitantes y que enmascaran así la linfocitosis del específico, que vuelve a presentarse tan pronto desaparecen aquéllas. Las observaciones números 13, 27, 28, 47, y 494 que citamos en nuestro trabajo, son ejemplos de lo que acabamos de decir.

IMPORTANCIA.

Del estudio de todas las observaciones que presentamos se deduce que la linfocitosis sanguínea reviste una excepcional importancia como signo que acompaña al específico, su presencia se hace evidente desde el comienzo de la infección, para acompañar al luético en su segundo y tercer período. La existencia constante nos ha llevado al convencimiento de que su determinación en la sangre, debe constituir desde aquí en adelante una investigación que se impone al médico en su examen clínico. La linfocitosis en su manifestación creciente, habiendo sido más o menos pronunciada antes del tratamiento, llega a un límite máximo. Cuando el enfermo es tratado convenientemente, tiende a descender hasta llegar a una cifra casi fija, siempre por en-

[1] Son solamente 500, las que citamos en el trabajo original.

cima de la cantidad normal Este descenso puede hacerse en forma gradual y más o menos rápido, o bien experimentar ciertas oscilaciones en la curva descendente, hasta llegar en su disminución a una cifra casi invariable.

VALOR.

La linfocitosis tiene mucho valor, en ocasiones, para hacer sospechar sífilis; nos referimos, entre otros, a aquellos casos en que una parturienta da a luz un hijo con suero-reacción de Wassermann positiva, en tanto que ella la presenta negativa. En estas circunstancias hemos podido ver que la linfocitosis sanguínea elevada, por arriba de la normal en la madre, demostraba que ella era una específica, capaz, por lo tanto, de engendrar un heredo-sifilítico. El tratamiento anti-luético materno nos ha mostrado a posteriori que tenía razón de ser la linfocitosis sanguínea elevada, desde que era capaz de reactivar la suero-reacción de Wassermann oculta.

En ocasiones, la linfocitosis se presenta en una forma casi aislada, de tal modo que si no tuviésemos otros indicios sobre su naturaleza podría pasar como un hecho banal o por lo menos sin explicación satisfactoria. Se hallan en este caso las observaciones 496 y 498, por ejemplo.

HEREDO-SÍFILIS.[1]

Su importancia es evidente, en la contribución que puede aportar al diagnóstico de la heredo-sífilis terciaria tardía, hasta hacer desaparecer dudas en algunos casos poco salvables y donde ella hará sospechar la etiología de las alteraciones clínicas observadas, especialmente en aquellos en quienes los antecedentes hereditarios son poco ilustrativos y las distrofías no muy aparentes. Desearíamos recordar aquí un trabajo de Gaucher en el cual, para llegar al diagnóstico de la heredo-sífilis se vale en unos casos de los antecedentes y en otros de las taras distróficas, ayudado una que otra vez por la suero-reacción de Wassermann y donde en todos los casos, el tratamiento específico instituído sirvió para confirmar la herencia sifilítica. Las dificultades del diagnóstico, serían mucho menores si se hubiera investigado la linfocitosis sanguínea.

En aquellos casos en que la lesión inicial se manifesta con caracteres poco precisos, pero que hacen sospechar el lues a punto de justificar un tratamiento abortivo, faltando todos los signos de la infección, la linfocitosis sanguínea, por su precocidad y constancia, autoriza la prosecución del tratamiento ante la posibilidad de una suero-reacción de Wassermann retardada y en tal sentido es digno de recordar las observaciones interesantes de Gougerot, que cita varios enfermos en quienes un tratamiento precoz e intensivo hizo retardar la suero-reacción hasta el 4°, 7°, y 9° mes.

REACTIVACIÓN.

Debemos señalar como un hecho interesante en el estudio de la linfocitosis de la sangre de los sifilíticos, su aumento provocado por la medicación específica, lo que se hace bien evidente cuando la proporción de linfocitos se aproxima a la cifra normal, lo que denominamos (como lo hace el Dr. Gourdy) en su tesis "reactivación de la linfocitosis." Esto, como lo hemos podido comprobar ahora, no es una consecuencia del medicamento, pues en los sujetos sanos y aun en los enfermos no específicos, no se produce.

PRONÓSTICO.

Como resultado del estudio de nuestras observaciones hemos adquirido la convicción de que la linfocitosis sanguínea no sólo tiene valor diagnóstico, sino que a la vez lo tiene en el pronóstico. Opinamos que la existencia de la linfocitosis sanguínea es una prueba de sífilis no curada; el hecho de que no existan síntomas clínicos nos dirá únicamente sífilis oculta o moderada por el tratamiento, pero pocas veces curada. Se nos podrá presentar, sin duda, sifilíticos que, tratados convenientemente, no presentan

[1]Debemos hacer presente que la linfocitosis sanguínea en la heredo-sífilis sólo tiene valor diagnóstico a partir de la segunda infancia.

ya manifestación clínica alguna, durante los varios años en que pueden tenerse noticias de tales enfermos, que no tienen suero-reacciones de Wassermann positivas, pero también no hay duda de que tales objeciones no dejan de estar sujetas a crítica y desde luego: ¿No es verdad que un sifilítico que se hizo tal cierto día, puede pasar varios años, diez y más, ignorada su infección, ignorado y sin tratamiento, desde la lesión inicial hasta las manifestaciones de tabes, parálisis general u otras?

REINFECCIÓN.

Para los que sostienen lo contrario y consideran curable la sífilis es argumento importante la reinfección. Pero hay que preguntarse si esas pretendidas reinfecciones son realmente tales o lejos de serlo son simples reavivaciones de la enfermedad, adormecida.

No es nuestro propósito entrar, en este resumen, a considerar los detalles que exponemos en el trabajo, tan solo tendremos en cuenta dos órdenes de hechos, unos clínicos y los otros experimentales. Entre los primeros debemos recordar los tres interesantes casos presentados á la "Société Française de Dermatologie" el 18 de Julio de 1911 por Bayet, Deneaux y Dujardin, en los cuales había aparecido una segunda sífilis con chancro, adenopatía y roseola, sin que hubiera habido nueva contaminación.

Por lo que se refiere a trabajos experimentales, citaremos las observaciones de varios autores competentes: Sandmann, en enfermos que habían sido intensamente tratados con mercurio y que se consideraban clínicamente curados, abandonan el tratamiento y después de mes y medio, y aún pasado el año no habían vuelto a aparecer síntomas algunos de especificidad; se les extirpó porciones de tejidos en los cuales anteriormente había habido localización específica e inyectándolos a ocho monos, ha podido ver el desarrollo de la sífilis.

Hoffmann, en idénticas condiciones de experimentación, ha llegado a las mismas conclusiones. Fischl, en virtud de sus observaciones, sostiene que las nuevas manifestaciones que podrían considerarse como debidas a una reinfección son debidas a multiplicación y pululación de los focos de espiroquetes que quedan en los tejidos; ha podido demostrar esto por sus experiencias: en ellas pone a contribución la cura intensiva combinada de neosalvarsán y mercurio, a pesar de lo cual ha podido revelar la existencia de espiroquetes en actividad en los sitios de la lesión primera.

TRATAMIENTO ABORTIVO.

En nuestro sentir, pues, el tratamiento abortivo no implicaría la esterilización del organismo a pesar de la excisión precoz del chancro, pues no libraría al organismo del proceso de infección general; sabiendo hoy lo que significa toda infección, aunque demore un tiempo más o menos largo en aparecer localizada, ha pasado por una faz septicémica. La sífilis, como todas las infecciones, al manifestarse luego en sus manifestaciones secundarias o terciarias, ha sido previamente una septicemia; también el chancro, clínicamente expresión primera, ha dejado transcurrir antes de él, un tiempo necesario, que, dado lo que dejamos expuesto en el concepto general de la patología de las infecciones, sería el período que la infección aprovecharía para generalizarse, mostrándose en un determinado momento, como primera aparición de enfermedad, al cual le acompaña la linfangitis, delatora del curso que aquella ha seguido.

NO CURABILIDAD.

Los autores que acabamos de señalar, al presentar experiencias en apoyo de la no curabilidad de la sífilis, lo han logrado merced a condiciones especiales que, para los que piensan de otro modo, podrían aparecer como excepciones; pero nosotros llegamos en apoyo de aquéllos, al invocar la linfocitosis sanguínea, que al manifestarse desde el momento en que la infección se establece, continúa con élla y no abandona al sujeto, dejando en él, el estigma indeleble de la infección luética latente, que atenuada

en su virulencia puede estar relegada a ciertos y pequeños focos por influencia del tratamiento, esperando el momento oportuno para exteriorizarse. Esta manera de encarar la infección luética por nosotros, nos lleva a sustentar aún hoy, la manera de pensar del viejo maestro, de Fournier, que desconociendo las reacciones biológicas, que para algunos serían las delatoras de la infección, preconizaba y seguramente, con verdad todavía para nosotros, que la sífilis necesita del tratamiento crónico e intermitente.

CONCLUSIONES.

El estudio detenido del tema que hemos desarrollado nos permite establecer cierto orden de conclusiones que sintetizan el espíritu de nuestro trabajo y que exponemos a continuación:

1°. La linfocitosis sanguínea es el signo más constante de la infección sifilítica; es precoz; comienza con la infección y acompaña la vida del sujeto; se encuentra en el heredo—específico (a partir de la segunda infancia).

2°. Los procesos infecciosos concomitantes, por pequeños que fueren, enmasçaran momentáneamente la linfocitosis sanguínea, dando polinucleosis; desde el momento que desaparecen, nuevamente se presenta aquella.

3°. La linfocitosis sanguínea como la suero reacción de Wassermann, pertenece a un reducido grupo de enfermedades. Los síntomas clínicos y las demás investigaciones de laboratorio, permiten excluir los otros procesos.

4°. Una fórmula hematológica propia corresponde a la linfocitosis sanguínea del sifilítico.

5°. La suero-reacción de Wassermann es más tardía en aparecer que la linfocitosis sanguínea.

6°. En las sífilis viejas, no tratadas, la suero reacción de Wassermann puede perderse. La linfocitosis sanguínea no se pierde.

7°. La linfocitosis sanguínea se reactiva con el tratamiento. Si por excepción, no existe desde el primer momento, la medicación la hace aparecer; si era escasa, la aumenta.

8°. La reactivación de la linfocitosis sanguínea es propia del específico, no depende de la medicación, pues ésta, por sí sola, no la provoca en sujetos no específicos.

9°. El tratamiento específico intenso y prolongado modifica la linfocitosis, sin llegar nunca a la normal.

10°. La linfocitosis sanguínea del sifilítico es una reacción biológica que seguramente significa persistencia del treponema pálido.

11°. La linfocitosis sanguínea, entre otros signos de laboratorio, impondrá el diagnóstico de sífilis, en los casos en que los síntomas clínicos faltan.

12°. La presencia de la linfocitosis sanguínea, en ausencia de suero-reacción de Wassermann, no implica la negación de sífilis, antes por el contrario, hará sospechar la enfermedad, e insistir en su investigación para aceptarla o excluirla según el resultado.

13°. La linfocitosis sanguínea corrobora que las afecciones tituladas hasta hace poco parasifilíticas, son de naturaleza específica.

14°. Que la linfocitosis sanguínea del específico se reactive con el tratamiento antiluético o disminuya con él, supone que su etiología es función de la presencia del treponema.

15°. La persistencia de la linfocitosis sanguínea, indica que la sífilis no se cura, que difícilmente desaparece o bien que, producida la infección luética (aunque menos probable), las condiciones anatomo-patológicas son tales que queda como un estigma de sífilis la producción anormal de linfocitos.

16°. El aumento espontáneo de la linfocitosis sanguínea del sifilítico, que casi siempre se observa a medida que nos alejamos del sifiloma y durante el período secundario, parece demostrar que depende de la pululación del espiroquete, provocando una reacción orgánica.

17°. La linfocitosis sanguínea puede ser el signo único de la sífilis conyugal en la mujer e indicar un tratamiento capaz de provocar la aparición de la suero-reacción de Wassermann oculta.

18°. La linfocitosis sanguínea es con frecuencia el signo único de la sífilis latente.

19°. La linfocitosis sanguínea puede ser el único estigma del heredo-específico (a partir de la segunda infancia).

20°. La linfocitosis sanguínea en un enfermo sospechoso de sífilis, tratado precozmente, antes de la aparición de la suero-reacción de Wassermann, permite continuar la medicación sospechando un Wassermann retardado.

21°. La linfocitosis sanguínea, no solo tiene el valor que le hemos asignado en el diagnóstico del lues, sino que también lo tiene en la profilaxia social; las amas, por ejemplo, con linfocitosis sanguínea elevada, hacen sospechar el lues y autorizan a profundizar la investigación. Si puesto en práctica un tratamiento de prueba (a pesar de no existir suero-reacción de Wassermann positiva) la linfocitosis aumenta, las probabilidades de infección son más evidentes.

22°. La linfocitosis sanguínea perdura como signo indeleble de sífilis.

23°. La persistencia de la linfocitosis sanguínea, a pesar de los tratamientos más enérgicos y prolongados, parece indicar que (con los descansos pertinentes) no debe abandonarse nunca la medicación.

24°. La linfocitosis sanguínea, después de todo nuestro estudio, resulta ser un complemento indispensable de la suero-reacción de Wassermann en el diagnóstico y una investigación necesaria para el pronóstico.

GRANULOMA VENÉREO [1]—CONTRIBUCIÓN PROVISORIA A SU ESTUDIO HISTOLÓGICO.

Por FEDERICO SUSVIELA GUARCH,

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DISTRIBUCIÓN GEOGRÁFICA.

Con el nombre de granuloma venéreo o groin ulceration, sclerotising granuloma of the pudenda, chronic venereal sores, granulome ulcereux des organes génitaux, etc., se ha designado en los últimos tiempos una afección, limitada a los órganos genitales o a su vecindad más próxima, ulcerosa, crónica y contagiosa.

La enfermedad ha sido descrita primeramente por Conyers y Daniels, en el este de la India, en la Guayana británica y por el último y más tarde en los Melanesios de las Islas Fiji, de las Nuevas Hébridas e Islas de Salomón. Demproolf describe una enfermedad de los Papúas y Melanesios en Nueva Guinea, que probablemente es la misma afección. Maitland, MacLeod y otros encuentran el granuloma en la India (Madrás, Calcuta, Assam). Goldsmith, en Palmerston (Australia del Norte). Los miembros de la expedición de la malaria, en el oeste de Africa.

La ulceración serpiginosa de los órganos genitales descrita por MacLeod (Ind. Med. Gaz., 1889), es la misma afección, reconocida por Patrich Masson, en el sud de la China. Taylor, de Nueva York, la ha encontrado en los blancos en los Estados Unidos. Pietro Sabela describe algunos casos en Trípoli, con el nombre de granuloma ulceroso de los órganos genitales.

El doctor Juan A. Rodríguez (Hospital Maciel, Montevideo) estudia actualmente varios casos de granuloma venéreo, que hará conocer próximamente.

[1] Nuestra contribución provisoria al estudio del granuloma venéreo con las observaciones recogidas en Montevideo, que nos proponemos ampliar e ilustrar muy próximamente, responde a aquella honrosa distinción, invitación del ministro de relaciones exteriores y al propósito de avanzar, si fuera posible, el conocimiento de un tema interesante de la patología humana.

E. Rabello Beaurepaire Aragão y Gaspar Viana, de Rio de Janeiro, han estudiado detenidamente el granuloma en la mencionada ciudad.

Según esta distribución, geográfica se ve que la enfermedad se halla extensamente repartida en los países tropicales y subtropicales.

EDAD Y SEXO.

El granuloma no ha sido observado antes de la pubertad; se le ha encontrado después de los 13 o 15 y hasta los 45 años. Ninguna raza parece ser excluída. Hombres y mujeres, pueden ser igualmente afectados, con preferencia la mujer.

CONTAGIO.

Hay álgunas razones para creer que la enfermedad es frecuentemente de origen venéreo. Maitland la ha observado en la boca de un marido y de su esposa. Él cree que pueda ser propagada al nivel de heridas de naturaleza veneriana.

Pietro Sabella, admitiendo el contagio sexual, lo ha encontrado, sin embargo, fuera de allí, en personas de menor edad, en familias de sus casos de Trípoli, lo que no es de extrañar por la promiscuidad impura e impropia de la vida en aquella población. Las ropas y las manos pueden haber sido el vector de trasmisión.

También Mense cree en esta autointoxicación, donde la ulceración viene a estar en contacto con la piel sana, como por ejemplo, en los pliegues anales y escrotales.

CARACTERES MACROSCÓPICOS Y SINTOMATOLOGÍA.

Tratándose de los caracteres macroscópicos, así como de la sintomatología del granuloma venéreo, nosotros traduciremos a continuación la descripción de Patrick-Masson y de Mense.

Según Patrick Masson, la enfermedad comienza, en la mayoría de los casos, al nivel de los órganos genitales, o del ano bajo la forma de un espesamiento o elevación de la piel, nodulosa, circunscrita e insignificante. La zona afectada está recubierta de un epitelio muy delicado, rosáseo y fácil de ser desprendido, se escoria pronto y deja desnuda una superficie que tiende a sangrar y a desollar, pero que no se ulcera de ordinario de una manera profunda. La enfermedad evoluciona, por extensión continua periférica y excéntrica y por autoinfección de una superficie contigua. En su extensión ella muestra una predilección por las superficies calientes y húmedas, particularmente los repliegues entre el escroto y los muslos, los grandes labios y los pliegues del ano. Evoluciona muy lentamente y emplea algunos años para recubrir una zona ancha. Conjuntamente con la extensión periférica, se forma una cicatriz densa retraída, desigual, que se desgarra fácilmente sobre la superficie recorrida por la activa excrescencia, más o menos nodulosa, que constituye el contorno de la formación patológica. A veces, algunos islotes de la parte activa del tumor aparecen en el tejido cicatricial, pero es al margen de la zona implicada que deben ser observados los caracteres especiales de la enfermedad. Cuando se trata de un tumor algo antiguo, encuéntrase una ancha zona de tejido cicatricial blanco o irregularmente pigmentado, algunas veces escoriado, que no tiene el aspecto de la piel sana, retraído, plegado o denso; la periferia irregular, estrecha y serpiginosa está constituída por tejido de nueva formación, noduloso, ligeramente elevado, rojo, barnizado, cubierta de una delgada película rosada, superficialmente ulcerada o agrietada.

En la mujer, la enfermedad puede extenderse a la vagina sobre los labios, y a lo largo de los pliegues del ano.

En el hombre, puede invadir el pene (comprendido el glande), el escroto, y la parte elevada de los muslos. En los dos sexos puede extenderse en algunos años al pubis, al periné y posteriormente hasta el coxis. A veces corre de la superficie del granuloma un líquido abundante, espeso, que ensucia los vestidos y emite un olor particularmente desagradable. En estas condiciones extiéndese la enfermedad lentamente, dura años, y da lugar a inconvenientes y a veces a alteraciones serias de parte de la uretra, de la vagina o del ano, pero sin perjudicar de otra manera a la salud del enfermo.

La descripción de Mense, no difiere de la anterior, tan bien detallada. Es de anotar, sin embargo, algunas particularidades de la misma. "No rara vez, dan los bubones supurados o chancros típicos, blandos iniciales, el punto de partida de la afección. (Conyers, Daniels, Maitland.) La pérdida de sustancia conduce a la

ulceración; los bordes sinuosos avanzan siempre adelante mientras que brotan en el fondo granulaciones que sangran fácilmente, túrpidas, rojo claras, brillantes, o gris mate, las que sobrepasan en los bordes el nivel de la piel, y se rehacen más tarde en el medio. El proceso continúa y ataca las mucosas vecinas, del ano, de la uretra y de la vagina; puede producir aún mismo una neoplasia heteroplástica en la profundidad y abrir la vejiga y el mismo abdomen. Las glándulas linfáticas, en lo general, no son afectadas. Los dolores son moderados."

Cuando la ulceración alcanza algún desarrollo, se retrae en algunas partes el tejido granular y prodúcense cicatrices y recubrimiento cutáneo. Las cicatrices sufren más tarde una considerable retracción, de tal manera, que originan estenosis rectales y uretrales. Pero en la periferia, avanza siempre, sin cesar, el proceso y parece dudosa una curación espontánea. Se han comprobado persistencias de diez años. Entretanto el estado general apenas es alterado y la nutrición se conserva bien. En los casos graves puede darse la muerte por anemia y pérdidas por vía de la secreción.

GÉRMENES DEL GRANULOMA VENÉREO.

Siendo nuestro estudio puramente histológico, no nos ocuparemos de la Bacteriología del granuloma venéreo.

Resumiremos, sin embargo, lo conocido hasta la actualidad:

Markham Carter, describe parásitos que considera como protozoarios. Elementos redondos u ovales. Algunos tienen forma de frijol.

Parece que estas formas son idénticas a las encontradas por Dónovan en 1905, en seis casos; él cree que se trata de protozoarios, cuya posición definitiva le parece dudosa. Los cuerpos eran de 1½ a 2 mm. y se hallaron en células epiteliales de la red de Malpighi y como macrófagos. Siebert ha descrito minuciosamente la forma en preparados, procedentes de allí, y también ha demostrado su presencia en preparados de Nueva Guinea; los toma por cocus, o células fermentos. Flu ha visto recientemente las mismas formas. Describe también masas plásticas que se asemejan a las descritas por Carter.

La posición definitiva de las formas cuyo conocimiento, sin duda, corresponde a Dónovan, no ha sido fijada definitivamente.

El germen de Dónovan ha tenido una comprobación en el Brasil, habiendo sido encontrado primero por E. Rabelo (1912), y después por Beaurepaire Aragão y Gaspar Viana, en 8 casos de su observación en Río de Janeiro, quienes lo han aislado y cultivado.

Trátase ya de pequeños cocus, rodeados de una cápsula, o de bacilos de extremidades redondeadas, rodeados también de una cápsula o sin ella. El germen es patógeno para los animales de laboratorio. No se comprueba la especificidad por el desarrollo experimental del granuloma.

M. Lennan describe en el granuloma venéreo un espirilo del tipo refringens y otra clase todavía desconocida. Wise encontró en 1907 espirilos del tipo de la palida, lo que indujo a Sabella, en Trípoli, a hacer inoculaciones de Salvarsán en dos casos con éxito curativo. Acland y Hickinbothan vieron espirilos con dos o tres ondulaciones, acumuladas a veces, diferentes a las de la sífilis, framboesia, *Ulcus tropicum*. Ese espirilo fué llamado por él "Espirilos aboriginales."

No se consiguió éxito en las inoculaciones del perro, cuyo animal se cree, en el vulgo, origina la transmisión a las mujeres. Castellani y Chalmers mencionan que en el perro se han encontrado tumores granulosos con espirilos. Bosanquet demostró también espirilos en cortes, según Levaditi, en el granuloma venéreo, en los naturales de Australia, numerosos, 3–4 milímetros bajo la superficie, en la base del granuloma.

El valor etiológico del *Sp. aboriginalis*, no está demostrado; quizás es sólo un parásito. Además, diremos que Siebert (1907) y Flu (1911) dan como causa etiológica otros microorganismos que vió primero Dónovan.

Por lo que precede, se ve que el problema etiológico no se halla resuelto desde el punto de vista bacteriológico.

EXAMEN HISTOLÓGICO DE NUESTRO CASO.[1]

En la orientación general, vese afectada la epidermis, el cutis y el subcutis, lo mismo que los elementos correspondientes en la forma que describiremos.

Las capas aisladas de la epidermis se hallan casi siempre más o menos reducidas, bajo deformaciones del conjunto, a la capa córnea, y esta misma limitada a un filamento frecuentemente desprendido, coloreado de amarillo naranja. Weigert van Giesson.

Por consiguiente, las capas de la epidermis no presentan sus relaciones recíprocas, ni la topografía ordinaria. Cuando existen, la capa germinativa, filamentosa y granulosa, y esto con las células alteradas, lo mismo que modificadas en su disposición, estructura y granulación, penetran a veces como desprendidas de la capa lúcida, en la forma de pequeños acúmulos que pudieran tenerse como brotes epiteliales neoplásicos por debajo del límite epidermis-corion, para confundirse con una infiltración linfocitaria vecina.

Además esas capas, en el caso de conservación, presentan de cuando en cuando espacios que contienen restos o detritus celulares. Esos espacios, a veces muy extendidos, alterando la red epitelial a la que dan formas caprichosas, encierran, además, del detritus, infiltración de linfocitos, del tipo de células plasmáticas linfocitarias, sobre un fondo de ligera masa de tejido colageno, que puede reconocerse como tejido conjuntivo joven, por su débil constitución fibrilar y sus núcleos. Toda esta alteración de la epidermis puede demostrarse muy claramente por medio del azul methyleno policromo de Unna.

La deformación de las capas de la epidermis enunciada y su alteración, hacen comprender la dificultad de poder encontrar alteraciones regulares en las células correspondientes. Sólo podemos anotar irregularidad de la capa germinativa, desprovista de las expansiones protoplasmáticas, dirigidas hacia el cutis, penetración de sus células en la capa filamentosa alteración de la estructura, mitosis; la capa lúcida aparece como la más conservada; por último, la capa córnea rara vez presenta sus núcleos ordinarios alargados; casi siempre se ha reducido a un filamento desprendido coloreado de amarillo anaranjado por Weigert van Giesson. En resumen, la epidermis parece ser el asiento de un proceso invasor y destructor dirigido de abajo a arriba.

El límite epidermis-corium, según lo precedente, carece de línea regular, y es el asiento de la infiltración linfocitaria, esparcida hacia el cutis y ocupando el lugar de las papilas. Estas hállanse dilatadas, apenas provistas de sus fibras ascendentes de tejido conjuntivo, pero ocupadas por la infiltración. No se encuentran vasos. Por debajo del límite epidermis-corium, se tiene una capa maciza, ancha, de infiltración, con prolongaciones hacia el cuerpo papilar. La masa de células de infiltración, comienza más abajo, en montones o acúmulos en el cutis, ocupando, como islotes, pequeños o grandes espacios. Estos espacios, pequeños o grandes, limitados, de 1 a 2 y hasta diez décimos de milímetro, por el tejido conjuntivo, se propagan hasta el subcutis. El tejido conjuntivo mismo del cutis y subcutis se muestra más espeso en el primero que en el segundo, tiene en el subcutis disposición ondulada irregular, paralelo, como de ordinario, a la superficie, presenta sus núcleos más o menos deformados grandes o vacuolizados. Es más bien tejido colageno. El tejido conectivo, encerrando lo mismo, en el cutis que en el subcutis, linfocitos, leucocitos y células plasmáticas linfocitarias.

Los vasos, más grandes, están espesados y principalmente su adventicia desaparece en la formación de tejido conjuntivo espeso, sin infiltración colateral; en cambio, la presentan los vasos pequeños (venas) en capa espesa circular. El semento endotelial, muchas veces conservado como se ve en los vasos cortados longitudinalmente. El lumen contiene restos de eritrocitos. Una acumulación extravascular de estos últimos, sólo se encuentra algunas pocas veces en espacios de tejido conjuntivo.

[1] El caso procede de la sala Germán Segura del Hospital Maciel, con que nos favoreció el Dr. Juan A. Rodrigues, cuya deferencia agradecemos.

Es difícil encontrar vasos linfáticos, y los que aparecen, hállanse envueltos en las células pequeñas de infiltración, y como si de aquí surgiera ésta.

No se encuentran otros elementos, como pelos, glándulas sudoríferas y sebáceas. Pueden percibirse, raras veces, restos de las glándulas, destruídas por la formación de tejido conjuntivo.

Hállanse células de núcleo polimorfo (serie leucocitaria).

Las células redondas de infiltración que figuran en nuestros preparados merecen una consideración especial por ser en su mayoría, fuera de linfocitos y pocos leucocitos, células plasmáticas linfocitarias y venir a ser por su dominio, a nuestra manera de ver, una característica del granuloma venéreo, como lo acentuaremos más adelante.

Sabemos que las células de orden linfocitario se dividen en linfoblastos y linfocitos. El linfoblasto (linfocito no adulto), tiene el tamaño de un mielocito, un protoplasma débilmente basófilo, núcleo bastante grande irregular, con una membrana proporcionalmente espesa y un núcleo más o menos tingible. Pegado al núcleo presentan los linfoblastos en general, una zona clara, que bajo la coloración de Altman-Schrider ofrece granulaciones groseras, de forma bacilar y color rojo. Estos linfoblastos que representan un estado de división de los linfocitos, presentan, por consiguiente, numerosas mitosis. Los linfoblastos aparecen más bien en la sangre, como prueba de funcionamiento exagerado del sistema linfático. Los linfocitos son pequeñas células con un núcleo redondo, rico en cromatina, presentando uno y hasta dos nucleolos, fuertemente tingibles.

También en estas células, hállase una zona clara alrededor del núcleo, en la que se encuentran granulaciones como en los linfoblastos.

(Las células grandes mononucleares, mostradas por Ehrlich con su triácido, son, en pequeña parte, linfocitos grandes, adultos, y en gran parte, formas de pasaje con núcleo poco lobulado.)

Ahora bien: las dos formas anteriores, los linfoblastos y los linfocitos pueden engendrar en los estados patológicos, las células plasmáticas linfoblásticas y linfocitarias. Las primeras, que sólo entran en consideración en pocos procesos se caracterizan por tener el núcleo propio del linfoblasto, un protoplasma más fuertemente basófilo y una zona más clara. Las segundas, o sean las células plasmáticas linfocitarias, son más importantes que las primeras, por constituir la masa principal celular, en la infiltración de pequeñas células.

Como primer carácter diferencial entre esas dos células tenemos en la célula plasmática linfocitaria, la forma de rueda del núcleo y su situación casi siempre más inclinado hacia el polo de la célula, la que es, en general, oval.

Además, en la parte del cuerpo celular a que se inclina el núcleo, hállase un área clara muy visible, con fuerte aumento y por la coloración de pyronina o de azul de methileno policromo de Unna, área que, coloreada por Altman-Schride, revela las mismas granulaciones que los linfocitos. No es raro encontrar en las células plasmáticas linfocitarias varios núcleos y hasta seis.

Todas las células del orden linfocitario (linfocitos, linfoblastos, células plasmáticas) tienen la propiedad de emigrar. Sin embargo, parece que sólo los linfocitos emigran en los vasos capilares, mientras que las otras células emigran en el tejido conjuntivo y al través del epitelio.

Ahora bien: como avanzamos antes, son las células plasmáticas linfocitarias las que hallamos en gran cantidad en la infiltración del granuloma, no sólo esparcidas hacia la periferia, vecindad del límite epidermis-corium, no sólo en los espacios lacunares anotados de las capas de la epidermis, sino también como acúmulos en espacios irregularmente formados, por fuertes fascículos de tejido conjuntivo. Encontrándose esas masas en la vecindad de los vasos, creemos que la emigración se da para el granuloma en el tejido conectivo. De todas maneras, el número tan considerable de células plasmáticas linfocitarias, y su vasta distribución parécenos, al menos según la constancia del fenómeno en nuestros preparados, una característica, no consignada hasta

ahora, según nuestras noticias, en el granuloma venéreo. Más adelante, expresaremos nuestra opinión sobre su origen y la influencia primaria que les asignamos en el proceso estudiado.

En resumen: el substractum, consiste al principio en una proliferación inicial de la epidermis, cuyos conos interpapilares se prolongan en una infiltración hasta interepitelial de células pequeñas, redondas, que vienen del corium (células plasmáticas). Los elementos ordinarios del corium, son reemplazados finalmente por células redondas, las que en su mayoría tienen el carácter de células plasmáticas linfocitarias, algunas linfoblásticas. Los vasos del cutis se encuentran dilatados. Por último, el epitelio superficial se atrofia y desaparece. La infiltración de células pequeñas es reemplazada por tejido conjuntivo joven y bajo formación activa vascular nace un tejido conjuntivo, espeso, granular, característico, que no presenta tendencia alguna a la degeneración purulenta o caseosa, no encontrándose células gigantes, ni células cebadas (Mastzellen). La acumulación de células plasmáticas, hace recordar al Plasmocytoma, tumor de células de ese orden, descrito por Schridde como extraña formación, ajena por su ubicación a todo origen medular.

DIAGNÓSTICO HISTOLÓGICO DIFERENCIAL.

Sólo un examen superficial ha podido confundir el granuloma venéreo, con el Cancroid de la piel, el lupus tuberculoso, el lupus vulgar y las formas elefantiásicas.

El Cancroid se caracteriza, desde luego, por la invasión neoplásica epitelial y por la presencia de las perlas cancroideas. El lupus tuberculoso, se revela por el tubérculo, cuyo examen bacteriológico basta para diferenciar los dos procesos, así como las células gigantes. El lupus vulgar se diferencia por sus células epiteloideas y células gigantes. Puede encontrarse a veces el bacilo de Koch. Sobre todo, el nódulo luposo, sufre la degeneración caseosa, y por lo mismo ofrece en su centro, un detritus o masa finamente granulosa, difícilmente tingible, con restos de núcleos que se colorean fuertemente. Las formas elefantiásicas de las partes genitales, nacidas a expensas de estados inflamatorios crónicos, diferentes de la *Elefantiasis arabum*, formas que siguen a la extirpación profunda de ganglios linfáticos, procesos cicatriciales, urogenitales y del recto, úlcera cruris, así como en el lupus y goma de la extremidad inferior, se distinguen por la formación en masa de tejido conjuntivo, con una falta casi completa de fenómenos irritativos.

Por el contrario de lo que pasa respecto de estas afecciones, el granuloma venéreo que hemos observado presenta relaciones cercanas con las lesiones inflamatorias de la sífilis, tales como el condiloma sifilítico, el chancro duro (Esclerosis inicial), el goma sifilítico o sifiloma de Wagner. Este último en su primer estado.

Si se estudia nuestro examen histológico se verá que ofrece el carácter general de las lesiones sifilíticas; constante infiltración de elementos jóvenes, en el seno del tejido conectio y perivascular, señalado por Ramón y Cajal. Haciendo luego la comparación particular, veremos que el ordenamiento del tejido conjuntivo, también perivascular, y los vasos mismos encontrado en nuestro tumor, se acuerda, con igual disposición señalada, para el condiloma sifilítico, por Ziegler y por Rieder. También los fascículos conectivos, descritos por nosotros preséntanse rellenados en sus espacios, por las células embrionarias mismas, como tiene lugar en el chancro duro. Por último, en el goma sifilítico, como en nuestro tumor, nace primero una formación neoplásica de tejido conectivo, perivascular, alrededor del cual se forma un infiltrado inflamatorio muy espeso. Alrededor de esta infiltración se dispone el tejido conjuntivo en láminas concéntricas. El goma se compone, por consiguiente, al principio, de una envoltura de tejido conjuntivo, de un infiltrado inflamatorio, y en el centro de éste, hállase nuevo tejido conectivo ricamente celular. El goma tiene, además, células epiteloidales y células gigantes. (Ehrman y Fick.)

Si se sigue el estudio de nuestro examen histológico, también se reconocerán dos circunstancias características, de gran importancia para la comparación de nuestro tumor, con las lesiones inflamatorias de la sífilis.

La primera se refiere al tejido conectivo, que ya hemos apreciado. La segunda, tiene que ver con la naturaleza de las células que constituyen en su mayoría, la infiltración, dando a estas lesiones una característica diferencial de la mayor importancia. Esas células sobre las que nos hemos extendido antes, y a que hemos llamado con Shride, células plasmáticas linfoblásticas y linfocitarias, reconocidas en nuestro tumor, son las mismas designadas con el nombre de células cianófilas por Cajal, y de células plasmáticas por Unna, en las lesiones inflamatorias de la sífilis; llamadas también por eso células específicas.

Tan sólo como diferencia pueden anotarse en las lesiones inflamatorias de la sífilis, y el granuloma que hemos estudiado, ausencia en este último de células epiteloides, y células gigantes. Pero la ausencia de esos elementos, por lo demás no siempre constantes, no compromete la analogía que establece la presencia de los otros, indispensables, como estructurales y topográficos.

CONCLUSIÓN.

Nuestro examen histológico, nuestro diagnóstico diferencial histológico y la comparación del proceso observado en nuestros preparados con las formas de inflamación sifilítica, nos llevan a considerar el granuloma venéreo, con cuya presencia se comprueba, en numerosos casos, la reacción positiva de Wassermann, como una forma de inflamación sifilítica.

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The CHAIRMAN. Before adjournment I wish to announce by way of record the title of the following reprint presented to the Congress through Section VIII:

Profilaxia social del delito, por Enrique Feinmann. Buenos Aires, Imprenta y casa editora de Coni Hermanos, 1913.

Adjournment.

SESSION OF SUBSECTION C OF SECTION VIII.

NEW EBBITT HOTEL,
Thursday morning, January 6, 1916.

Chairman, GEORGE M. KOBER.

GENERAL TOPIC:

Pan-American Theme: "Etiology and prevention of tuberculosis from a sociological standpoint."

The session was called to order at 9 o'clock by the chairman.

Papers presented:

Contribución al estudio de la etiología y profilaxis de la tuberculosis desde el punto de vista sociológico, by Nicolás A. Solano.

La tuberculosis en Bolivia; su etiología y profilaxia, by Néstor Morales Villazón.

Profilaxia de la tuberculosis, by Constancio Castells.

La tuberculosis en el Uruguay, by Joaquín de Salterain.

"A tooth is more valuable than a diamond," by Felipe Gallegos.

CONTRIBUCIÓN AL ESTUDIO DE LA ETIOLOGÍA Y PROFILAXIS DE LA TUBERCULOSIS DESDE EL PUNTO DE VISTA SOCIOLÓGICO.

Por NICOLÁS A. SOLANO,
Miembro de la Asociación Médica de la Zona del Canal.

PARTE I.—ETIOLOGÍA.

HERENCIA.

La herencia, atributo esencial de la vida y cuya acción sobre la constitución del ser es tan palpable, ha ejercido a través de los siglos inmenso predominio en lo que pudiéramos llamar la génesis patológica.

Su historia en la enfermedad que nos ocupa ha atravesado fases muy diferentes y contradictorias que, haciendo doctrina, explican las contradicciones que, al correr del tiempo, ha habido en la profilaxis de dicha enfermedad. Así vemos que Hipócrates hacía de ella toda la etiología de la tuberculosis al sentar su principio absoluto: "Un tísico nace de un tísico," y que Broussais siguiendo su camino definía la tuberculosis: "Es una enfermedad orgánica diatésica y hereditaria." Esta manera de considerar la etiología de la tuberculosis fué un poderoso enemigo de las sabias medidas profilácticas dictadas en los años 1751 y 1790 por los reyes Fernando VI de España y Felipe IV de Nápoles, respectivamente, y aún hoy forma criterio y conserva casi todo su vigor en la humanidad.

La herencia de la tuberculosis ha distraído, pues, la atención de la clínica en todo tiempo y al advenimiento de la bacteriología los trabajos de laboratorio no se han mostrado indiferentes a la solución del problema.

Bien es cierto que la infección del óvulo por el espermatozoide ha sido demostrada por criadores que han logrado obtener terneros tuberculosos de vaca indemne y toro contaminado, probando así la tuberculosis concepcional, en el caso raro pero posiblo de que llegue al útero junto con el gérmen fecundante el microbio patógeno y que este tome alojamiento en el embrión. Este caso aunque se hayan citado ejemplos en la raza humana debe ser considerado excepcional, puesto que el bacilo tendría que alojarse en la cabeza del espermatozoide, y disminuiría cuando menos la vitalidad de este dadas sus dimensiones respectivas: 4 por 3 micros para el primero y 5 por 3 micros para el segundo.

El caso de madre tuberculosa y padre indemne es mucho más frecuente y se explica naturalmente por la íntima conexión que existe entre el organismo materno y el del embrión o feto, constituyendo un caso de generalización de la tuberculosis, ya que existan lesiones patológicas en la placenta, o porque los bacilos arrastrados por los leucocitos fuera de su foco primitivo—digamos el pulmón—atraviesan la red placentaria a la manera de los otros elementos de la sangre y van a continuar su desarrollo en un punto del organismo del feto, generalmente el hígado, produciendo así la enfermedad en él. En ambos casos no hay herencia de tuberculosis, como lo expuse en mi tesis de grado, sino contagio intrauterino o generalización, que impropiamente se ha llamado herencia del grano o heredo-contagio.

El papel que desempeña la herencia en la etiología de la tuberculosis no es, sin embargo, despreciable, ya que es un hecho comprobado que esta enfermedad no anida allí donde el organismo le ofrece, en virtudde su vitalidad normal, alguna resistencia; y que naturalmente un ser formado por la fusión de dos células (óvulo y espermatozoide) en que ambas o una de ellas está herida de decadencia orgánica, del mismo modo y por el mismo efecto que lo están todas las células del organismo de un tuberculoso de que provienen, darán nacimiento a un ser débil y de receptividad mórbida positiva. El conjunto de atributos anatómicos, químicos y dinámicos transmitidos por herencia al nuevo ser lo harán apto para el contagio, el cual tiene mayor probabilidad de ejercer su influencia nefasta que en cualquiera otro proveniente de organismos sanos. Es pues una herencia de predisposición lo que contemplamos en la mayoría de los casos seguida de un contagio por el modus vivendi actual. Esto se llama heredo-predisposición.

Aún la heredo-predisposición, si atendemos a los datos estadísticos de Pidoux, quien deduce de ellos que la tisis no nace de la tisis sino en 20 por ciento, lo cual se conforma también con las opiniones de Hallopeau y Apert, tiene una importancia menor que el contagio en la propagación de la tuberculosis; más, aún, generalmente el niño viene al mundo sin manifestaciones de tuberculosis y la enfermedad en estos heredopredispuestos no se manifiesta sino en épocas alejadas de la del nacimiento, cuando ya no se puede seperar la idea del contagio, puesto que ha sido lactado por su madre tuberculosa y se ha criado en un medio tuberculígeno por excelencia. Y es que en este caso particular de la herencia, como en ella considerada en general, el medio modifica los caracteres y más aún las receptividades mórbidas, que en el organismo han imprimido sus ascendientes; de ahí que los individuos de ascendencia no tuberculosa estén más expuestos a contraer la enfermedad cuando se uncuentran sometidos al contagio,que los de cepa tuberculosa a los cuales se sustrae de ese contagio.

Nuestra idea al respecto es, pues, que la herencia tuberculosa en toda la acepción de la palabra, es decir, que el tísico nazca del tísico, es rara y que la herencia de predisposición a la tuberculosis es muy frecuente y la que se observa en casi la totalidad de los casos.

CONTAGIO.

Historia.—El bacilo de la tuberculosis, descubierto por Robert Koch (quien lo hizo conocer el 24 de marzo de 1882 por medio de su comunicación titulada; "Nota sobre la investigación y cultivo del bacilo de la tuberculosis," dirigida a la Sociedad Fisiológica de Berlin, y que contiene la descripción, manera de aislar, cultivar y diferenciar

el microorganismo de la enfermedad que nos ocupa), había sido presentido por los sabios de mediados del siglo XIX; en efecto Villemin, en 1865, demostró la posibilidad de la transmisión de la tuberculosis por inoculación y con esa previsión que constituyó su mayor gloria, declaró: "El tubérculo es el resultado de la presencia de un virus en el organismo y la inoculación de él no obra por la materia visible y palpable que entra en el producto patológico, sino en virtud de un agente más sutil que se encuentra contenido en él y que escapa a nuestros sentidos."

Mas la idea del contagio no data desde los trabajos de Villemin; en el siglo II de nuestra era Galeno hablaba de transmisión de la tuberculosis de un individuo a otro. Rhases y Avicenne en el siglo X opinaban de la misma manera. Silvius descubrió el tubérculo en el año 1555 y sus contemporáneos Fallope y Montano aceptaban el contagio por cohabitación. Fracastor (siglo XVI) reconoce el contagio y es el primero en tratar el asunto de manera científica y detallada. Después vienen Morton, Valsalva, Van Swieten, Frank, Morgagni. Morgagni y Valsalva llevaron sus ideas hasta creer nociva y peligrosa la autopsia de un tísico y no la practicaban nunca. Morgagni sentó este aforismo "Phtisicorum cadavera fugi adolescens, fugio etiam senex" y de él hacía partícipes a sus alumnos; precaución que decía, parecerá exagerada pero es la más segura. Baumes y Hufeland participaban de esta opinión. Esto en cuanto al mundo científico.

Como iniciativa gubernamental encontramos la de Fernando VI, ya citada, la cual reflejaba, naturalmente, la idea arraigada del contagio en el pueblo español en esa época. He aquí el decreto fechado el 6 de octubre de 1751 en el Palacio del Buen Retiro y refrendado por el primer Ministro Zenón de Somodevilla, Marqués de la Ensenada:

Habiendo demostrado la experiencia cuan peligroso es el uso de la ropa de cuerpo muebles y objetos que han pertenecido a personas atacadas o fallecidas a consecuencia de enfermedades éticas, tísicas y otras contagiosas, ordenamos expresamente a todos los médicos de hacer conocer las enfermedades o muertes de tisis.

De modo que el alcalde haga quemar la ropa de cuerpo, los vestidos, los muebles y todos los objetos al servicio personal del paciente y que hubieran quedado en su habitación.

Que el alcalde ordene también que la habitación donde el enfermo hubiere fallecido sea revocada y blanqueada: que el piso o enlosado de la pieza o de la alcoba sea rehecho.

Además se abrirá un registro en el cual se inscribirá la procedencia de las ropas existentes en casas de cambalaches o mercaderes de ropa vieja, con indicación de los nombres y domicilio del vendedor, así como de aquellos a quienes las ropas y vestidos hubieran servido, cambalacheros y ropavejeros haciendo el comercio ordinario de efectos contaminados.

El alcalde entregará un papel atestando que las susodichas mercaderías están exentas de contagio: lo que permitirá a los interesados retener o vender las mercaderías de ocasión.

Todo médico que no declare al alcalde de su cuartel las enfermedades o fallecimientos tísicos incurrirá: por la primera vez, en una multa de 200 ducados y suspensión durante un año; por la segunda vez multa de 400 ducados y la pena de destierro por cuatro años.

Todas las personas o enfermeros, criados o gentes al servicio del tísico, que no hagan la declaración, incurrirán en la pena de 30 días de encarcelamiento, por la primera vez; de cuatro años de presidio por la segunda.

Las autoridades civiles, religiosas y militares tendrán que hacer quemar en los hospitales civiles y militares toda la ropa de uso de enfermos y soldados tísicos.

Mas las teorías de Broussais desviaron esta corriente de preservación así como las posteriores de Nápoles ya citadas, corriente que era como una predicción del immortal descubrimiento de Koch. Laennec al contrario aconsejaba preservarse para evitar el contagio. Después viene Villemin, quien con sus trabajos y su predicción da la noción del contagio exacta, confirmada por el descubrimiento del bacilo, que clasifica la tuberculosis al lado de la fiebre tifoidea, el cólera, etc., es decir, hace de ella una

enfermedad general infecto-contagiosa de la cual es necesario y posible preservarse y a lo cual se tiende hoy universalmente.

Vías del contagio.—Es este otro punto que ha suscitado discusiones numerosas y en que las conclusiones a que han llegado los diferentes experimentadores están lejos de un acuerdo perfecto. Para nosotros descartada la penetración del microbio por la herencia en la forma que dejamos expuesta al tratar de ella, el bacilo tuberculoso puede penetrar al organismo por tres vías, la sanguínea por la inoculación, la digestiva por la digestión, y la aérea o bronquio-pulmonar por la inhalación.

La tuberculosis por inoculación es rara: ella ha permanecido en la esfera de las investigaciones de laboratorio y presta allí preciosos y decisivos servicios a la clínica. Fuera de esta esfera se observan raros casos de tuberculosis por inoculación accidental, causadas por heridas durante las autopsias y disecciones anatómicas. En la literatura médica se registra el caso de Laennec, quien se hirió uno de los índices aserrando unas vértebras tuberculosas, lo cual dió lugar a una tuberculosis localizada que luego se generalizó. Estos casos se hallan localizados entre los estudiantes de medicina y los mozos de morgue.

El contagio por inhalación e ingestión es más frecuente, casi los únicos medios que se observan en la vida diaria; se discuten aún la preponderancia en la propagación de la tuberculosis y a sus numerosas discusiones se han consagrado más de una vida y más de una década, sin que al presente inhalatorios e ingestionistas hayan cejado en solucionar el problema del lado de sus contenedores y respondiendo con teorías y experimentos a las teorías y experimentos que vienen a quitarles su preponderancia.

Pasemos una rápida ojeada sobre unas y otras ya que de ellas hemos de deducir necesariamente las medidas preventivas.

Tappeiner, Reech, Koch, Nocard, Flügge, Kuss se encuentran entre los inhalatorios: así Tappeiner nos dice que, de sus investigaciones, la inhalación de aire contaminado produce la enfermedad; Reech refiere una observación clínica de tuberculosis adquirida por insuflación de aire contaminado en el recién nacido: Una comadrona tuberculosa tenía la costumbre de aspirar las mucosidades de los recién nacidos de boca a boca y practicaba de igual modo la insuflación y 10 niños cuidados por ella murieron de meningitis tuberculosa; Koch inhala cultivo de bacilo tuberculoso diluído en agua destilada en la tráquea de animales y todos presentaron lesiones claras de tuberculosis a pesar de haberlos colocado en las mejores condiciones higiénicas; el Profesor C. Flügge de Breslau concluye de sus investigaciones que la infección tuberculosa por las vías respiratorias es, sin duda, más fácil y más grave que la infección por vía digestiva. Apoyándose en estas investigaciones de Flügge, dice la Memoria de Maggoon y Barnet de Cuba:

Es posible producir experimentalmente la tuberculosis pulmonar en varios animales (curies, conejos, cabras, terneros, perros), haciéndoles inhalar aire mezclado con gotitas de agua que contengan bacilos de Koch. En estas condiciones bastan a veces pocos bacilos (50 y hasta menos) para provocar la aparición de lesiones tuberculosas en el pulmón. La inhalación también parece ser un medio de infección superior aun en rapidez a la infección subcutánea no obstante ser ésta tan eficaz. Por otra parte, se puede demostrar con facilidad en estas investigaciones que por la inhalación los bacilos han penetrado en realidad hasta los bronquios más pequeños: para ello se inoculan al curi en seguida de la inhalación, fragmentos completamente periféricos del pulmón del animal que haya servido para el experimento. Los curies sucumben con mucha rapidez después de estas inoculaciones. Por el contrario, cuando los bacilos se introducen en el organismo del animal mezclados con los alimentos se necesita una masa enorme de bacilos para obtener síntomas de infección tuberculosa. La infección, así como el resultado final, se produce mucho más tarde.

Es errónea, por consiguiente, la opinión de algunos autores, de que los bacilos inhalados sólo obran cuando una parte de ellos ha podido pasar directamente al tubo digestivo por la faringe. Pudiera sostenerse mejor la opinión opuesta, esto es, que los experimentos de tuberculización por los alimentos que han sido eficaces, débense a que se ha producido una aspiración de partículas alimenticias aún infinitesimales, que

han bastado, por los bacilos que contengan para provocar una infección bronquial más o menos rápida. Por otra parte, el Profesor Flügge no ha podido conseguir nunca la infección tuberculosa de un animal cuando le introducía directamente, por medio de una técnica especial, los alimentos mezclados con bacilos en el estómago o en el intestino.

Si experimentalmente los peligros de infección por inhalación son mucho mayores que los de infección alimenticia, no es posible señalar en definitiva sin otras investigaciones, a cual corresponde la preponderancia de uno o de otro de estos dos modos de infección en la tuberculosis adquirida espontáneamente. Sería conveniente, por el contrario, investigar cuales son, en las condiciones habituales de la vida, las oportunidades de infección para una u otra vía.

Se ve que la tuberculosis por la vía respiratoria conserva toda su importancia, pues por frecuente que sea la entrada de los bacilos tuberculosos en el intestino, no sufre aquella grandes efectos si nó se ha efectuado al mismo tiempo la introducción de los mismos por medio de la inhalación.

Los medios de infección son muy diversos para el hombre y los animales domésticos. Cuando el curi o el ternero se alimentan con leche de vacas tuberculosas, se observa casi constantemente que la infección se verifica por vía intestinal; pero el Profesor Flügge expresa que aún así la tuberculinización ha podido producirse por la respiración directa de gotas de leche bacilíferas. En estos casos puede considerarse como excepcional la contaminación por el aire.

Los animales que hayan escapado de la infección intestinal pueden adquirir la tuberculosis por inhalación, en la proximidad de vacas tuberculosas que lanzan partículas bacilíferas.

En el hombre la infección se verifica de maneras muy variables, debidos a las costumbres de los individuos. Los niños por ejemplo, pueden ingerir bacilos en la leche, la mantequilla, o llevándose a la boca los dedos sucios con esputos. El profesor Flügge observa y con razón que el peligro para los niños aumenta según la proporción mayor de vacas afectadas y con la falta de cuidado y señala la incuria natural de los tísicos, por lo cual se cree que bastaría tomar precauciones elementales para preservar a los niños supuesto que la cantidad de bacilos que pudiese llegar al intestino, sería insuficiente en la gran mayoría de los casos para provocar la infección.

De lo expuesto se deduce: que la inhalación de aire bacilífero es la fuente más abundante de la infección y que basta una cantidad muy pequeña de bacilos para provocar la tuberculosis.

Los ingestionistas han llevado por su parte, observaciones clínicas y experimentos en apoyo a la primacía de la infección por las vías digestivas. Tomemos las observaciones de Calmette de Lille, tanto por ser las más recientes cuanto por haber tenido en cuenta rodearse de las mayores precauciones para alejar toda causa de error. Dice Calmette:

"Desde hace muchos años esta cuestión es el objeto principal de investigaciones de laboratorio que prosigo con ayuda de mis discípulos y en particular, de C. Guerin. Ella preocupa igualmente a un gran número de investigadores en todos los países. Y no es de los menos apasionados, así como lo atestiguan las discusiones de nuestros congresos.

Hace cuarenta y tres años, Villemin nos enseñó que la tuberculosis es inoculable y contagiosa, y 26 años nos separan de la época memorable en la cual Robert Koch, al descubrir y cultivar su bacilo, hizo la demostración de su especificidad.

A pesar de la enorme acumulación de trabajos publicados en este último cuarto de siglo, no hemos fijado sino muy imperfectamente la importancia respectiva de las diversas vías por las cuales el virus tuberculoso puede penetrar en el organismo del hombre y de los animales sensibles. Hasta en estos últimos tiempos el mayor número de sabios, clínicos y experimentadores, consideraban como dogma intangible el origen respiratorio de la tuberculosis pulmonar y los resonantes debates que tuvieron lugar en las conferencias internacionales de la Haya en 1906, de Viena en 1907, y desde entonces en diversas sociedades de sabios, están muy presentes en nuestro espíritu para que haya utilidad alguna en recordarlas. De ellas se desprende evidentemente la impresión de que un acuerdo definitivo está próximo a establecerse, y que como siempre la verdad no se encuentra en los polos.

Si parece innegable en ciertos casos, probablemente rarísimos, que la infección directa del pulmón por el aire respirado puede efectuarse, a pesar de las múltiples líneas de defensa acumuladas en esta vía, es manifiesto que el camino normalmente seguido por el virus tuberculoso para llegar hasta el parenquima pulmonar es, lo

más a menudo, la circulación linfática o sanguínea, por la gran puerta de entrada del tubo digestivo.

La experimentación demuestra que, para realizarse la tuberculización primitiva del pulmón por la vía aérea, es preciso colocarse en condiciones extra fisiológicas, como lo han hecho Nocard y Flügge y más recientemente Kuss, al inmovilizar animales para obligarlos a respirar durante largo tiempo una atmósfera cargada de polvos infectados líquidos o secos. Los polvos líquidos muy finos son seguramente peligrosos, sobre todo para los niños; y parece evidente que las neumonías gaseosas primitivas y las tuberculosis pulmonares agudas de la primera edad son casi siempre, de origen respiratorio. Cuando una madre o nodriza, afectada de tuberculosis pulmonar clásica, tose o estornuda a corta distancia de los labios de un niño de pecho que respira con la boca abierta o grita en espera del seno que debe alimentarlo, el contagio por inhalación es casi fatal. Pero para el niño de más edad y para el adulto, este modo de contaminación es seguramente excepcional.

Más excepcional aún es la infección por los polvos secos y los experimentos positivos de Cornet, como los de Kuss, efectuados encerrando animales inmovilizados en un espacio cerrado lleno de una nube de polvo de talco o de restos de fibras vegetales mezclados con esputos secos, no niega en manera alguna los resultados negativos, mucho más numerosos, señalados por Baumgarten, Tappeiner, Cadeac, Mallet, Paterson y por mí con Vansteenberghe.

La asepsia de las vías respiratorias ¿no atestigua altamente la eficacia protectora de sus medios de defensa cuando éstas no están atacadas por alguna lesión preexistente del conducto naso-faringeo, de la laringe y de los gruesos bronquios?

La adenopatía traqueo-bronquial primitiva que ciertos autores consideran siempre como originaria de una infección respiratoria, no puede ya ser invocada como un argumento probatorio en favor de ésta.

Si es exacto, según la ley de Parrot, que es siempre acompañada o precedida por uno o muchos tubérculos pulmonares, nada prueba que éstos sean de origen aerógeno, porque se presentan con extrema frecuencia en los animales artificialmente infectados por el tubo digestivo. Por mi parte lo he observado regularmente con M. Breton, en un gran número de curies a los cuales había hecho absorber por el recto o ingerir con la sonda esofagiana una pequeña cantidad de emulsión fina de cultivo puro de bacilos tuberculosos bovinos. A menudo estos animales, sacrificados después de cuatro o cinco semanas no presentaban otras lesiones que uno o dos tubérculos superficiales del tamaño de una cabeza de alfiler, ocultos en uno de los lóbulos anteriores del pulmón y a los cuales correspondía un enorme infarto del paquete ganglionar peribronquial. Un observador que ignorara las condiciones en las cuales se había efectuado la infección experimental, habría afirmado, sin duda alguna, que se trataba de una contaminación respiratoria.

Es pues incontestable, que si la tuberculización primitiva del pulmón o de los ganglios traqueo-bronquiales por inhalación directa de polvos bacilíferos es manifiestamente posible en algunas casos, ella es excepcional.

El estudio atento del contagio tuberculoso en los animales suministra abundantes pruebas clínicas del predominio de la infección por las vías digestivas.

Se sabe, por ejemplo, que los carnívoros, tales como el león, el tigre, la hiena o el chacal, contraen a menudo la tuberculosis de forma pulmonar u visceral en nuestros jardines zoológicos cuando se les alimenta con carnes tuberculosas, mientras que estos animales no contraen la tuberculosis en estado salvaje. El perro se tuberculiza cuando ingiere los esputos de su amo tuberculoso; el ternero, el gato y el cerdo contraen la tuberculosis cuando se les alimenta con leche rica en bacilos.

Se ha insistido con justicia, en estos últimos tiempos, sobre la ausencia completa de tuberculosis en los cerdos alimentados exclusivamente con maíz u otras substancias vegetales sometidas a la cocción, mientras que esta enfermedad es extremadamente frecuente allí donde se hace consumir a los cerdos residuos no pasteurizados de las lecherías.

Es evidente que la tuberculosis que se desarrolla así, a menudo con lesiones primitivas de la pleura o de los ganglios bronquiales, en los cerdos alimentados con leche de vacas tuberculosas, resulta de la absorción de bacilos por el tubo digestivo. Lo cual es debido a que estos bacilos ingeridos pueden atravesar las paredes del intestino, entrar en la circulación linfática y sanguínea y ser arrastrados por ella, más o menos tiempo, antes de producir en el organismo los desarreglos característicos de la infección tuberculosa.

Experimentalmente ha sido demostrado primero por Chaveau, de 1865 a 1876 después por Villemin, Aufrecht, Gerlach Kleps, Gunther y Harms y muchos otros observadores, entre los cuales conviene citar, sobre todo a Saint Cyr, Viseur, Bollinger, Orth, Toussaint, Baumgarten, Ravinovitch, Parrot, Ravenel, Schroeder y

Cotton, etc. Por otra parte otros hechos negativos resonantes, particularmente los publicados por Colin (de Alfort) y por Moeller, parecen demostrar que los animales pueden tragar impunemente grandes cantidades de sustancias tuberculosas. Conocemos hoy la razón de ello: es que la infección artificial del tubo digestivo no se realiza con seguridad sino cuando se toman ciertas precauciones que he precisado con G. Guérin; es necesario hacer absorber los bacilos en estado de división tal, que queden finamente emulsionados como lo están en los esputos o en la leche. En estas condiciones, una sola comida infectante basta ordinariamente para producir lesiones tuberculosas que, en los animales jóvenes, permanecerán a menudo localizadas, por mayor o menor tiempo en los ganglios mesentéricos y que, en los adultos aparece al contrario primitivamente en los pulmones.

Al estudiar el mecanismo de la absorción de polvos inertes por la mucosa intestinal, he podido comprobar con Vansteenberghe, que se observan los mismos hechos. La ingestión de polvos finos de negro de humo, o mejor de tinta china mezclados con alimentos, produce en el curi adulto las lesiones típicas de la antracosis pulmonar, mientras que en el curi joven los granos coloreados permanecen más o menos tiempo en los ganglios mesentéricos. Los cortes de fragmentos de intestino delgado, fijados durante la digestión, permiten entonces reconocer estos granos coloreados englobados en los leucocitos y en los vasos quilíferos de las vellosidades.

Al repetir nuestras investigaciones a este respecto, Sir William Whitla y Simmers han hecho recientemente las mismas comprobaciones y estos sabios indican un procedimiento ingenioso que les ha permitido realizar simultáneamente la tuberculosis y la antracosis de los pulmones o de los ganglios mesentéricos; este procedimiento consiste en hacer absorber a los curíes jóvenes o adultos una emulsión mixta de bacilos tuberculosos y de tinta china en aceite de olivas.

La experimentación sobre los grandes bovídeos permite establecer, con mayor certidumbre aún, el trayecto que siguen los bacilos tuberculosos para llegar hasta los pulmones si se sacrifica cada animal, como lo he hecho con C. Guerin, en épocas más y más alejadas de la única comida infectante. Puede uno convencerse entonces que estos bacilos, así como lo había demostrado Chauveau y después Dobroklowski, atraviesan la mucosa intestinal aunque esté intacta, y que no dejan en ella, en la generalidad de los casos, ninguna huella de su paso. Son transportados por los leucocitos polinucleares desde los vasos quilíferos de las vellosidades hasta los ganglios mesentéricos más vecinos.

En los animales que aún maman y el niño de primera edad, son frecuentemente retenidos en estos órganos linfáticos, que desempeñan respecto a la linfa el papel de un filtro casi perfecto. Ya los bacilos acaban por destruírse allí a la larga, ya crean en estos órganos lesiones tuberculosas que evolucionan hacia la caseificación, vertiendo sus microbios en los canales linfáticos eferentes, o algunas veces en el peritoneo.

En los individuos de mayor edad, cuyos ganglios mesentéricos, como lo ha demostrado Weigert, son mucho más permeables, los bacilos—siempre englobados en los leucocitos polinucleares—son arrastrados en la linfa del canal torácico hasta el ventrículo derecho del corazón y propulsados en los capilares del pulmón. Si los leucocitos parasitados han perdido sus movimientos amiboideos a consecuencia de su intoxicación (que resulta de la tuberculina secretada por los bacilos), son incapaces de atravesar por diapedesis las paredes de estos capilares y crean entonces finas embolías que llegarán a ser el punto de partida de otras tantas formaciones tuberculosas a expensas de las paredes endoteliales vasculares (granulaciones grises de Laënnec).

Las lesiones tuberculosas así constituídas evolucionan en seguida, sea hacia calcificación, sea hacia la caseificación. En la segunda alternativa, los tubérculos se vacían en los alvéolos o en algunos vasos linfáticos o venenosos, con mayor rareza en una arteriola. Entonces determinan una diseminación más o menos rápida y más o menos grave de virus en otras regiones del organismo.

En mis investigaciones con C. Guérin he comprobado siempre la extrema frecuencia de la adenopatía traqueo bronquial en los bovídeos de poca edad cuando los bacilos han franqueado el filtro ganglionar meséntrico y ganado los pulmones. Esta adenopatía está en relación constante con una o muchas lesiones tuberculosas subpleuríticas que son fáciles de descubrir.

El origen digesti o de estas lesiones es del todo evidente. Las hemos reproducido muchas veces y Vallée (de Alfort) las ha obtenido igualmente, sea alimentando terneros con leche de vacas tuberculosas, sea inoculando directamente los bacilos en un ganglio mesentérico después de laparotomía.

Nos ha sido posible observar, además, en algunos de los animales infectados por las vías digetivas, localizaciones primitivas de la tuberculosis en otros órganos que los ganglios mesentéricos o el pulmón.

La hemos visto aparecer bajo forma de pleuresía, de artritis, de orquitis y en un caso muy notable, en un cabrito, bajo forma de iritis. Estas localizaciones excepcionales no sobrevienen sino en animales infectados una sola vez con débiles cantidades de bacilos. Se puede pensar que éstos, en razón de su pequeño número, han quedado largo tiempo en circulación en la sangre, arrastrados por algunos leucocitos polinucleares y han acabado por constituir una lesión tuberculosa solamente en el órgano en que estos leucocitos se encontraban cuando han sido heridos por la muerte.

Cualquiera que sea la interpretación que se dé a estos hechos, permanece cierto que la tuberculosis pulmonar llamada primitiva y que muchas otras formas o localizaciones de la infección tuberculosa, resultan manifiestamente, en gran número de casos, de la penetración del virus por la vía digestiva.

Los partidarios convencidos del predomio de la inhalación sobre todo Flügge en Alemania, Kuss en Francia, objetan que para producir experimentalmente la tuberculosis por ingestión es preciso hacer absorber a los animales millares o millones de bacilos, mientras que algunas unidades de éstos bastan para producir lesiones tuberculosas del pulmón cuando son inhalados.

Los que piensan así se olvidan con frecuencia que de los millones de bacilos ingeridos, sólo un pequeño número—algunas unidades, sin duda—logran atravesar la mucosa intestinal, y que la mayor parte de los que la franquean son destruídos ulteriormente en los ganglios mesentéricos. Finalmente, pocos de entre ellos son arrastrados por los leucocitos al torrente linfático del canal torácico y de allí a los capilares del pulmón. Pero aquéllos que llegan hasta él, determinan entonces esas formaciones tuberculosas intravasculares tan bien descritas por Borrel, después por Letrelle, y cuya lenta evolución, por accesos sucesivos, acaba por crear la tisis.

Si tantos médicos se obstinan en creer que frente al contagio tuberculoso el hombre se comporta de manera distinta que los animales, es quizá porque las viejas ideas sobre los miasmas pesan aún sobre nuestros cerebros.

Sin duda, algunos de ellos nos han exagerado la importancia y la frecuencia de la contaminación del hombre por la leche, y aquellos que sostienen hoy que la tuberculosis se contrae por el intestino con mayor frecuencia que por las vías respiratorias, sufren la pena de estas exageraciones.

Así, debemos protestar contra esa tendencia a identificar el origen intestinal con el origen alimenticio. Ciertamente, para nuestra especie, el hombre es—no me cansaré de repetirlo con insistencia—el principal factor en la propagación de la tuberculosis. Pero creo que es preciso afirmar vigorosamente que, si el hombre puede tomar excepcionalmente la tuberculosis, sobre todo en la primera edad, por inhalación de bacilos, la contrae con mayor frecuencia por la absorción intestinal, a menudo y largo tiempo repetida, de algunos bacilos acabados de expulsar por un tuberculoso.'

Como se ve de lo que dejamos transcrito, de las tres vías por las cuales el mibrobio tuberculoso penetra en el organismo, la sanguínea por la inoculación es la menos frecuente y también la más fácil de evitar; y de las otras dos consideramos cierta pero accessoria, afortunadamente, la infección por inhalación, y decimos afortunadamente porque como dice Flügge, la llegada de polvos contaminados, secos o húmedos, al pulmón por inhalación, no sólo produce seguramente la tuberculosis, sino que su forma es de las más graves; y si la inhalación tuviera el predominio en la etiología de esta enfermedad, como lo quiere éste, la proporción de la morbilidad y mortalidad tuberculosa sería en extremo alarmante ¿Quién no ha estado sometido alguna vez a la acción de polvos baciíferos diseminados en el aire? ¿Los mismos experimentadores podrían ponerse al abrigo de la contaminación al manejar esos polvos secos casi impalpables e imperceptibles? Ahora la experiencia diaria nos presenta casos frecuentísimos de focos tuberculosos familiares en que la mayoría de los convivientes del tuberculoso escapan a la infección, y esto no obstante estar todos sometidos a la misna aereación. Queda pues la ingestión como la más frecuente de la vías de la infección tuberculosa, por la gran puerta de entrada del tubo intestinal.

Medios de contagio.—De una manera general, todo producto de excreción o de secreción que contenga el bacilo de Koch, es un medio de contagio.

Lo contienen generalmente, el esputo, las materias estercorales, la orina, la esperma, etc., cuando son emitidos por un tuberculoso de las vías respiratorias, del intestino, del aparato uro-genital, etc., respectivamente y el pus de los abcesos tuberculosos. El bacilo de Koch arrastrado al medio ambiente por estas secreciones o excreciones, puede

encontrar ocasión de penetrar en un organismo indemne pero receptivo y constituir así un medio de contagio.

Cornet dice: "el esputo y especialmente el esputo seco, es la sola causa de la propagación de la tuberculosis pulmonar;" Villemin había, 13 años antes del descubrimiento de Koch, indicado con su admirable perspicacia el papel que desempeñan los esputos en el contagio.

El esputo bacilífero es el medio más frecuente de contagio, ya sea que desecado y pulverizado venga a mezclarse con el aire ambiente y penetre excepcionalmente en los bronquios o los alvéolos pulmonares, o que contamine los alimentos o que de cualquiera otro modo llegue en estado de división extrema al intestino.

Durante largo tiempo se ha considerado la opinión de Cornet como axiomática. Hoy, según las nuevas investigaciones, ésta pierde su predominio en favor de la del esputo fresco, acabado de expulsar:

El Profesor Flügge insiste sobre el peligro que presentan las partículas de la expectoración de los enfermos lanzadas durante la tos, y las considera como la fuente de infección más común, sobre todo en el momento en que se arrojan. Según él es mucho más rara la infección debida al polvo de los esputos desecados. El peligro por la proyección de la tos de gotitas bacilíferas, es de extrema frecuencia; adquiere mayor importancia aún en las relaciones de madre a hijo, de enfermos con enfermeros, de los cónyuges entre sí, de los obreros con sus compañeros.

La causa más frecuente, más eficaz, de la propagación de la tuberculosis es el producto de los tísicos en el instante mismo de su emisión. (Maggoon y Barnet, Memoria citada.)

El Profesor Calmette es de opinión también que el esputo fresco es el agente principal de la propagación de la tuberculosis, y a él debe incriminarse la extensión de la enfermedad por sobre cualquier otro medio de contagio:

El peligro es infinitamente mayor y más frecuente por los bacilos de origen humano recientemente salidos del pulmón de un enfermo, cuando son transportados de los esputos a nuestros alimentos o a la mucosa bucal por el contacto directo o indirecto de la boca, de las manos, de los objetos contaminados o de las moscas. La madre tuberculosa que prueba el potaje destinado a su hijo o que le enjuga la cara con su pañuelo, la nodriza que lubrifica el seno con su saliva, el niño que toca sus alimentos después de haber paseado sus manos sobre los pisos, el adulto que moja sus dedos llevándolos a la boca para hojear un libro, para manejar caracteres de imprenta o para servirse de instrumentos que pertenecen a tuberculosos que arrojan bacilos, ingieren a cada instante algunos microbios virulentos y los riesgos de contaminación son para ellos tanto más graves cuanto que estas ingestiones son más abundantes y más repetidas.

Los bacilos que contiene el esputo acabado de emitir pueden ser transportados a nuestros alimentos por los insectos. La mosca, ese insecto casero que nos acompaña por doquiera, que pulula allí donde nuestros alimentos se encuentran, que llena, en ciertas estaciones del año, de una manera insólita comedores, cocinas, calles y sobre todo en la exposición alimenticia sin abrigo a la contaminación, que llamamos mercado, es uno de los elementos más eficaces para la propagación del contagio: ella se posa sobre los esputos, ingiere cantidad de ellos y parte lleva en sus patas para luego abandonarla en los alimentos y contaminarlos de este modo. No sólo es peligrosa la mosca por que acarree el bacilo, sino también porque al morir y pulverizarse puede dejar un residuo que, contiene el bacilo de Koch si ha ingerido esputos bacilíferos, y es infectante. Sus excreciones también lo contienen y pueden obrar a la manera de sus cadáveres, mezclándose al aire ambiente y contaminando nuestros alimentos o los objetos de nuestro diario y reiterado uso. Si tenemos en cuenta, además, las largas excursiones que ellas hacen, se comprende el amplio papel que desempeñan como medio de propagación de la tuberculosis y de otras enfermedades infecto-contagiosas.

Si bien es cierto que en algunas de nuestras ciudades de la América Hispana, se han dictado medidas sanitarias para contrarrestar el peligro de la mosca, en la gene-

ralidad de ellas no ha dado el resultado apetecido, debido a que no se da el público cuenta exacta de lo que esas medidas significan y por ello son mal acogidas por los vendedores de sustancias alimenticias, los cuales desean tener siempre a la vista del público sus artículos de expendio.

La chinche, tan común en las poblaciones de clima tropical, también ha sido incriminada de trasmitir la tuberculosis.

Los animales domésticos también pueden ser contaminados por el bacilo humano y a su vez constituir un medio de contagio. Tenemos una observación del Dr. Tascón, el cual la tomó en el Hospital San José de Buga.

Una enferma atacada de tuberculosis pulmonar aguda tenía una inapetencia absoluta, por lo cual sólo tomaba poquitos de leche, y contra mi expresa voluntad, le daban las sobras a un gato que criaban en dicho hospital con mucha estimación. Poco tiempo después cuando aún vivía la enferma, aquel pobre animal empezó a revelar los síntomas característicos de una tuberculosis pulmonar, por lo cual hube de sacrificar el animal y comprobado el contagio hice incinerar el cadáver, para evitar que a su vez constituyera un encadenamiento de propagación de la enfermedad.

Bien conocida es esa extraña manera de proceder, de las mujeres sobre todo, con los animales domésticos, ya se trate de un falderillo, de un gato, de un loro, etc., en que la extravagancia las lleva hasta besar y alimentar de boca a boca a dichos animales.

Esta práctica trae consigo que si dichos animales contraen la tuberculosis, como en el caso arriba transcrito, la trasmiten seguramente a sus dueños o allegados de éstos. El peligro de esta convivencia es mucho mayor cuando se trata de gentes de baja clase, pobres, habitantes de bohardillas.

La observación que hemos transcrito es, además, muy fértil en enseñanzas, y nos indica que no sólo el esputo del tuberculoso es nocivo, sino también su saliva, ya que restos de ésta fué la que infectó la leche, y no puede ser de otro modo puesto que la boca es el camino normal y reiterado de los bacilos que salen del árbol aereo. De ahí que la opinion del Profesor Flugge sobre la importancia de "las partículas de la expectoración de los enfermos lanzadas durante la tos," la hagamos extensiva a las partículas de saliva, producto más fluído y por consiguiente más fácil de pulverizarse por la corriente de aire expirado.

La contaminación por las materias estercorales del tuberculoso, toma amplia parte en el contagio en nuestras ciudades y aldeas donde estas materias son arrojadas a pozos ciegos o derramadas sobre el suelo; las moscas, y los animales domésticos que sirven a la alimentación humana pueden contagiarse y continuar los eslabones de la cadena de contagio.

El bacilo de Koch, huésped de un individuo tuberculoso, penetra a veces nuevamente en su organismo después de haber sido expulsado de él, e infectar un aparato u órgano hasta entonces indemne; es lo que se llama auto-infección. En el estado actual de nuestros conocimientos y en consecuencia con las opiniones del Profesor Calmette, siguiendo estos bacilos la misma vía que sus predecesores se localizan en otro punto del organismo, porque encuentran allí, ya sea por un estado patológico posterior a la infección tuberculosa, ya por que herido el organismo de decadencia vital por la acción de toxinas del bacilo, un *locus minoris resistentiae* o se deja invadir en cualquier punto atacado, privado como se halla de sus medios de defensa.

Está fuera de discusión que el bacilo humano produce la tuberculosis en los animales no refractarios a ella y con tanta rapidez y seguridad en algunos de ellos, como el curí, llamado por esta razón animal reactivo. Los animales a su turno trasmiten su tuberculosis al hombre.

Sobre el tapete científico se encuentra aún la cuestión de identidad o dualidad de los bacilos tuberculosos en el hombre y los animales domésticos. Este asunto ha sido objeto de numerosos trabajos de parte de los experimentadores y el origen de

numerosas discusiones científicas en distintas corporaciones, sin que a la hora presente se haya llegado a una solución satisfactoria entre las opiniones extremas.

En 1901 el ilustre Koch hacía conocer solemnemente estas dos conclusiones: (1) La tuberculosis humana difiere de la tuberculosis bovina y no puede ser trasmitida a los ganados; y, (2) la trasmisión al hombre de la tuberculosis bovina por la leche o la carne, es apenas más frecuente que la tuberculosis hereditaria: por consiguiente, no es necesario tomar medida alguna para contrarrestarla.

Estas conclusiones del sabio más eminente en materia de tuberculosis, dieron lugar a numerosos trabajos contradictorios. Youg, Fibiger, y Arloing, establecen la identidad de la tuberculosis humana y bovina y no hacen diferencia entre las dos que la de mayor virulencia del bacilo bovino. Gratia declara la identidad de todas las tuberculosis. Bujwid y Perroncito son partidiarios de la dualidad. Löffler, Kossel, Pfeiffer y Waserman admiten la infección posible, muy rara además, del hombre por el bacilo bovino, pero sostienen la teoría de su maestro Koch.

La mayoría del Congreso Internacional de Higiene, reunido en Bruselas en 1903, sin estar en favor de la identidad de los bacilos en las diferentes especies animales, cree necesario prescribir medidas contra los peligros de contagio, posibles para el hombre, de la tuberculosis bovina.

Lignières, quien acepta con la mayoría de los experimentadores el peligro del contagio para el hombre, de la tuberculosis bovina, termina en su estudio titulado "La tuberculosis humana y la de los animales domésticos," con estas conclusiones, que si no resuelven el punto de identidad, si merecen tenerse en cuenta, considerada la cuestión desde el punto de vista profiláctico:

Las tuberculosis verdaderas encontradas en el hombre y en los animales domésticos se deben a bacilos pertenecientes todos al mismo grupo, a la misma especie: al bacilo de Koch, que sufre la ley general de la variedad de los tipos.

Así es que a más de las variedades posibles y todavía indeterminadas, conocemos ya los tipos diferentes, a saber: el bacilo tuberculoso tipo bovino que sólo es una variedad del tipo humano, o viceversa; los bacilos tipo aviario y tipo pisciario, que son razas distintas entre sí y entre los tipos humano y bovino.

Ya que el bacilo tuberculoso del bovídeo puede infectar al hombre, sobre todo a los niños de corta edad, y aunque esta contaminación parezca por ahora excepcional, sería una culpa grave abandonar la lucha tan sabiamente reglamentada contra la tuberculosis bovina. Es preciso, al contrario, proseguirla, completarla y extenderla todavía a las demás tuberculosis animales, no sólo para contrarrestar el posible contagio al hombre, sino al mismo tiempo, y de ello se olvidan muy a menudo, para combatir las tuberculosis animales, particularmente la bovina, que tiende a difundirse cada vez más en los ganados.

El Dr. Gache, en su libro titulado "La tuberculosis en la República Argentina," llama la atención acerca de la propagación de la tuberculosis por la carne de los bovídeos, y Arloing citado por él, hace notar que la disminución de la tuberculosis humana en Lyon y su aumento en Burdeos, por ejemplo, podría muy bien deberse a la mayor severidad de la inspección de carnes en la primera ciudad.

El mismo Dr. Gache nos dice que los criadores de la Argentina han comprobado que los animales tuberculosos se encuentran siempre entre los de media sangre, es decir, que resultan del cruce de animales indígenas con importados:

Durante la época que precedió a la importación de animales, la tuberculosis no se encontraba sino excepcionalmente en el rebaño argentino, pero desde hace algunos años, desde que se ha comenzado a mejorar la raza introduciendo toros y vacas Durham y Jersey, etc., esta enfermedad está muy esparcida y su difusión progresa en íntima relación con el grado de afinamiento. Así pues, a medida que el cruce hace perder al rebaño argentino sus condiciones primitivas para darle un aspecto bello y esbelto de que carecía, sus cualidades de vitalidad se debilitan, su organismo degenera, su energía y su resistencia disminuyen. Es un triste privilegio que los animales de rango elevado han incorporado a nuestra principal fuente de riqueza, al mezclar su sangre azul a la sangre roja, criolla, de los de las praderas argentinas.

Estas comprobaciones del Dr. Gache han sido observadas también en algunos otros puntos de la América Latina, entre otros en Bogotá por el Dr. Federico Lleras A.

Pero si la tuberculosis bovina no es frecuente en nuestros países y por consiguiente el peligro de contaminación al hombre por ella es casi nulo, no lo es que él existe por la contaminación de las carnes y sobre todo de la leche por el bacilo humano. En la generalidad de los casos la carne y la leche puede contaminarse por el bacilo humano desde el matadero o el establo hasta el lugar de consumo, ya que o no hay inspección sanitaria, o la que existe es tan deficiente que a veces constituye un peligro mayor, que si no existiera. Es notorio el desaseo de los matanceros, su falta absoluta de conocimientos higiénicos; lo mismo sucede con los acarreadores de carne, con sus vehículos y accesorios.

Entre este personal no es raro encontrar individuos que sean tuberculosos o al menos que padezcan de enfermedades del árbol aéreo (poitrinaires, que dicen los médicos franceses). Puede comprenderse el immenso peligro que existe con este *modus vivendi*, si se considera además que el personal veterinario, salvo ligeras excepciones es de una incompetencia absoluta. Este peligro de contaminación es mayor para la leche, medio de cultivo por excelencia para la generalidad de los micro-organismos, puesto que los lugares de expendio de este artículo de primera necesidad reunen todas las condiciones para una fácil y segura contaminación: tienduchos donde se barre al seco, hay aglomeración, y adultos y niños con enfermedades del pecho. Aún para las ciudades que tienen una inspección de carnes, existe el peligro de las foráneas, ya que la salazón puede disimular y disimula en ocasiones a las carnes contaminadas, tal como el expendio de ella se hace en la generalidad de nuestras ciudades. Nosotros consideramos pues, el peligro de la carne y de la leche no desde el punto de la tuberculosis bovina sino de la contaminación de estos artículos por el bacilo humano, obrando a la manera de vehículos trasportadores del bacilo de un individuo enfermo a otro sano, del mismo modo que el pan, en cuya elaboración toma parte un personal alcohólico, que trasnocha constantemente y que se tuberculiza fácilmente.

CONTAGIO EN LOS DIVERSOS MEDIOS SOCIALES.

1. *La familia.*—El tuberculoso cuidado en su casa es hoy el más terrible agente para la propagación de la tuberculosis, no sólo para los suyos, sino también para todos los que lleguen a tener con él algunas relaciones. Cuando se presenta en un miembro un caso de tuberculosis pulmonar, se llama al médico en los ataques agudos; él prescribe lo necesario para contener la tempestad del momento; alivia mas no cumple la alta misión que le está encomendada: salvar del peligro inminente la vida de los allegados del enfermo, por las siguientes razones: o cree que no debe alarmar a la familia del paciente indicándole la gravedad del mal, presentándole el cuadro sombrío que está en gestación, aunque no le sea desconocido el valor del silencio; o si así lo hiciere el hablar de cambio total de vida, de separación del enfermo y sus allegados bajo el peligro de contagio, encontrará, en la generalidad de los casos, resistencia de parte de ambos: del primero por no abandonar su vida de comodidad o de lujo, si se trata de un rico; porque es menester el trabajo diario para el sustento de los suyos, si no lo es, y del segundo porque puede oponerse a conveniencias sociales, a asuntos de interés; o porque un altruismo mal entendido hace imposible la separación, juzgando los temores del médico exagerados o innecesarios. Esto hace que el contagio sea un hecho inexorable. En casos muy raros el médico es un individuo de espíritu recto, altruista en el sentido estricto de la palabra, entonces puede entablarse la lucha entre él, la familia y el paciente, y si al fin logra imponerse, generalmente es ya un poco tarde: el germen del contagio ha tenido tiempo de echar sus cimientos.

El médico prescribe durante el ataque agudo, la escupidera con solución desinfectante o sin ella; esto último es la regla general, pero después que el enfermo se levanta, que vuelve a sus quehaceres, sus esputos van a ensuciar el suelo, las paredes, etc., de su alojamiento, de su gabinete o taller, diseminando aquí y allá

innumerables bacilos, que transportados por las moscas o más tarde por la pulverización de los esputos extendidos en capas delgadas por los pies o la alcoba, van a infectar a otros de los que cohabitan con él. El tuberculoso se sienta a la mesa común sin que en la mayoría de los casos, haya separación alguna entre los cubiertos, servilletas, etc., de su uso y si la hubiere, es de resultados nulos puesto que los objetos serán lavados en común con los demás. La desinfección previa es cosa que nadie conoce ni se preocupa de ello. El tuberculoso cuidado en su casa, generalmente vaga de consultorio en consultorio antes de que se le haga un diagnóstico positivo, o que al menos se le informe de ese diagnóstico y de los peligros que su enfermedad puede traer a su familia.

En toda familia donde existe un tuberculoso aún avanzado éste recibe de sus allegados, madre, esposa o hija, los alimentos que prueban con el mismo cubierto del enfermo, muchas veces después que éste los ha llevado a la boca, unas veces para hacerle ver que están bien preparados o apetitosos y otras para hacer ostentación de que su estado no les inspira temor o repugnancia. Los niños de la casa reciben sus caricias y la familia en general permanece algunas horas del día en su cuarto, a veces sentada en la misma cama del enfermo haciéndole compañía en medio de un aire contaminado por las partículas de esputo y de saliva que se diseminan en el ambiente durante los accesos de tos, y a las cuales el Profesor Flügge da una importancia capital en la propagación de la enfermedad. Para el médico es en verdad duro privar a un individuo próximo a abandonar la vida, de las últimas fruiciones familiares: ¿pero no lo es más contemplar con la estoicidad de un cómplice que el flagelo extienda sus negras alas sobre un grupo de seres a quienes se puede salvar de sus garras? Rodearse del valor necesario para hacer comprender el peligro, es la tarea del médico, escabrosa en verdad, por la resistencia que encontrará de parte de la familia y del enfermo; pero del cumplimiento de la elevada misión que le está encomendada por magisterio de su profesión depende el éxito de ella. De esta manera se enseña al tuberculoso a hacer profilaxis no sólo para los suyos, sino también para él mismo, evitándole infecciones secundarias, y con la esperanza de que los suyos no serán contaminados, debe además inculcársele fe en la curabilidad, en algunos casos, porque ello sea de esperarse dados los medios con que se cuente, y en otros como un lenitivo moral indispensable; es seguro que pondrá todo su contingente al servicio de la ciencia y luchará por el triunfo de ella, ya que luchar es un sentimiento innato en la humanidad.

"El médico," como dice el profesor Granchet, "debe al enfermo la verdad, toda la verdad" y creemos que ella solamente dé los resultados que acabamos de anotar. Además del contagio directo por el tuberculoso cuyos esputos pulverizados van a mezclarse con el aire, impregnando las ropas de su uso, las de su cama, infectadas, ya porque escupa en ellas o porque durante los accesos de tos se ensucie con las partículas de esputos, éstas van al lavadero con las de los individuos sanos, y por consiguiente serán un medio de contagio tanto para su familia, como para la encargada de lavarlas; porque si como es el caso, generalmente, la lavandera se encuentra agotada por el trabajo, alcoholismo, tabaquismo, mala alimentación, tenemos en ella un candidato seguro para la tuberculosis y para propagarla entre los suyos y los que a ella ocupen.

Como se ve el encadenamiento de este orden de cosas no puede ser mejor establecido para la propagación del contagio.

El aseo en las habitaciones en nuestras ciudades se hace generalmente por medio del barrido al seco lo cual levanta nubes de polvo que van a depositarse sobre los muebles, libros; si se trata de un comedor sobre los alimentos que están destapados o mal protegidos, sobre la vajilla o resto de ella, para después servirse de ellos sin precaución alguna. Ya se comprende el peligro que esta manera de proceder acarrea puesto que el traumatismo de los pulmones por el polvo absorbido aun no bacilífero crea en ellos una menor resistencia en su tejido y aumenta el peligro de contagio si las alfombras, pisos, etc., se encuentran contaminados por esputos bacilíferos. Cuando

el tuberculoso muere generalmente no se prescribe la desinfección y si la familia no ha sido aleccionada sobre la conducta que debe observar respecto a los objetos de uso del enfermo, como también es de regla general, y además arraigada la idea de la herencia morbosa siendo casi desconocida la manera de propagación por el contagio, los objetos propagadores de éste, sin desinfección previa van a servir a los sobrevivientes o se regalan a los menesterosos, que llevan en su limosna un medio de acabar más pronto su existencia. De esta manera se van desarrollando esos focos que la humanidad llama hereditarios y que en verdad no son sino contagio. Casos de éstos son observados por los médicos do todos los países, para que haya interés alguno en citar ejemplos.

Este contagio en el medio familiar es mucho más frecuente y más alarmante cuando se trata de la familia obrera, Y la razón es obvia: basta echar una ojeada sobre la vida del obrero en casi todas las ciudades de alguna importancia, para comprender que son aptos para recibir y propagar todas las epidemias y endemias.

El obrero vive generalmente aglomerado en casas donde las condiciones higiénicas brillan por su ausencia: generalmente son tugurios donde se respira al mismo tiempo el humo de la cocinilla mezclado al ambiente de excreciones humanas y de animales que habitan con él, perro, gato, gallinas, en hacinamiento indescrifrable de personas, animales y cosas; el salario es exiguo, cuando no falta del todo, y de ahí la miseria, el alcoholismo, causas todas, que como lo veremos más adelante, hacen el terreno orgánico de esas familias de una receptibilidad asombrosa para el desarrollo del bacilo de Koch. Esto lo hemos podido comprobar a nuestro paso por los servicios hospitalarios.

2. *Hospital.*—Los hospitales policlínicos son perjudiciales desde el punto de vista de la tuberculosis, no sólo para el enfermo atacado de ella sino también para los otros enfermos.

Los hospitales policlínicos de caridad no tienen disposiciones relativas a la profilaxis de la tuberculosis, hay allí generalmente aglomeración y no están construídos en lugares apropiados para la cura de la tuberculosis.

La mortalidad allí por esta enfermedad es a veces asombrosa: en el Hospital San Juan de Dios, de Bogotá alcanzó en el año de 1896 el tercio de la mortalidad adulta. La hospitalización de tuberculosos en promiscuidad con los enfermos atacados de otras lesiones hace que aquella enfermedad tome esos caracteres alarmantes que imponen imprescindiblemente, un cambio radical de costumbre, si es que algo merece nuestra atención la clase obrera que va allí en busca de refugio y de alivio a las dolencias de la vida.

Estos hospitales son un contra sentido no sólo para el tuberculoso sino tanbién para los enfermos atacados de otras lesiones, puesto que allí encuentran diseminados el bacilo de Koch que germinará en sus organismos receptivos, como lo son todos los de los individuos que buscan un refugio en estos establecimientos.

Hay más, el tuberculoso no siempre es un inválido; él no busca el hospital sino cuando su enfermedad le impide trabajar por lo muy avanzada o por un ataque agudo, frecuente en los casos de tuberculosis pulmonar; repuesto de él, sale a la brega por la vida, sin haber recibido las instrucciones convenientes a su estado, repartiendo por doquiera los productos del laboratorio que lleva en sus pulmones y dejando el puesto infectado al que llega.

Puede darse una idea de los peligros que este género de hospitalización acarrea, si se tiene en cuenta que de esos hospitales salen individuos de todas las profesiones y oficios en número no despreciable, el cual corresponde en su mayor parte al grupo de oficios domésticos.

3. *Ejército y marina.*—En los países que tienen servicio militar obligatorio, los médicos se encargan hoy de rechazar los individuos que presentan alguna tara orgánica y excluyen los que estén afectados de tuberculosis, pero en los países en que la recluta se hace de manera empírica se comprende fácilmente que el soldado lleve al cuartel las epidemias de su lugar natal y que al obtener su libertad importe a éste las enfermedades que reinen en el cuartel.

Propiamente hablando los cuarteles no se han construido en la generalidad de los países latinoamericanos teniendo en cuenta los preceptos de la higiene. El personal es en general analfabeta y la vida se hace allí en promiscuidad. Y no es raro con este *modus vivendi* que lleguen tuberculosos al cuartel y propaguen la enfermedad entre sus camaradas.

La generalidad de los enfermos en un cuartel son atendidos allí en enfermerías o trasladados a un hospital, de donde vuelven en estado de convalecencia nuevamente a su cuartel entre los cuales no es raro encontrar enfermos tuberculosos. En el año de 1908 pasaron en este estado al ejército acantonado en Bogotá 7 individuos atacados de tuberculosis pulmonar y 12 de otras formas: es decir enfermos en impotencia de contagio y otros los cuales por las condiciones de medio, aglomeración, la disciplina que los obligará a prestar servicios allí donde la necesidad lo exige, poco importa que sea de noche y a la intemperie, no opondrían mayor resistencia a la tendencia invasora del bacilo de Koch.

No sólo el cuartel es perjudicial al soldado tuberculoso, éste también es perjudicial al cuartel y en mayor escala, si se tiene en cuenta el número de víctimas que la enfermedad puede hacer por la acción del contagio.

El soldado tuberculoso lleva al cuartel el grano, bacilo de Koch, que ha de germinar en un terreno apto ya que el reclutamiento en la forma forzosa lleva al ejército individuos de la baja clase social en las ciudades y a los campesinos, habituados al aire libre a la luz, en todo a un género de vida totalmente distinta de la urbana y más aún de la de cuartel, que lo deprime moralmente, y este decaimiento de ánimo que sufren las gentes del campo, así como las demás circunstancias anotadas, hacen que opongan una menor resistencia a las enfermedades infecto-contagiosas en general y a la tuber culosis de manera especial cuando son transplantadas a las ciudades, viniendo a ser, como dice el Dr. Gache los autores de esta verdad de Lancereaux: "La tuberculosis es la enfermedad de la civilización."

4. *Talleres.*—Un representante dijo, con mucha razón, ante el Consejo de vigilancia de Asistencia Pública en París: "Hay talleres en que de antemano se ha establecido el lugar del tísico. Cuando uno no puede ya ocuparlo, viene un sucesor y así se suceden en el mismo lugar series de obreros contaminados por sus predecesores."

El peligro en estos medios como en toda colectividad, es el esputo, peligro que hace más positivo el estado del terreno.

En los talleres no hay hasta hoy, escupideras y los esputos lanzados al suelo son luego esparcidos sobre el utilaje por el barrido en seco y así como, lo hemos visto, llevan los obreros esos útiles a la boca o sus manos son ensuciadas, el contagio no es de dejarse esperar. Esos útiles empleados por un tuberculoso lo serán después de su retiro del taller por su reemplazo, cuando no son de uso común, como sucede con las vasijas del agua.

Estas mismas observaciones tenemos que hacer respecto a las oficinas públicas.

5. *Escuelas y colegios.*—Generalmente lo único que nos preocupa es la instrucción y poco o nada la educación física, por falta de conocimientos de las leyes fisiológicas. El organismo es un todo armónico compuesto de partes muy diversas; cada una de ellas tiene su función, en verdad distinta, pero siempre em correlación íntima con las grandes funciones de ese todo. Que una de ellas llegue a perder o simplemente a alterar su estado normal y el todo sufrirá necesariamente la falta de aquella. Así, sin el desarrollo físico normal, sin la integridad de las funciones de la vida animal, las de la vida psíquica no podrán dar el trabajo indispensable que en el estado normal del organismo. De ahí que en las agrupaciones de los internados sea poca la atención que la higiene se merece, siendo allí de necesidad imperiosa, no sólo para preservar a los educandos de las enfermedades infecto-contagiosas, sino también, y he aquí el gran papel a que está destinada en la prosperidad, para enseñarles a hacer profilaxis individual y que a su vez la establezcan en sus hogares. El movimiento antituber-

culoso del mundo entero, contará en el porvenir con ese grande ejército, si se implantan en todos los establecimientos de enseñanza, las medidas contra esta enfermedad.

La vida común durante varias horas o varios meses que existe entre los escolares hace destacar claramente la posibilidad de contagio entre ellos, así como también entre los maestros, si no se ha tenido cuidado de seleccionar el personal.

6. *Teatros, etc.*—La vida urbana nos lleva buscar en los lugares públicos, teatros, cafés, cantinas, salas de baile, prostíbulos, etc., un cambio de decoración, o un mayor ensanche a nuestras viviendas estrechas. Sin saber que en la mayoría de estos lugares podemos encontrar un contagio por la falta de escupideras y la comunidad de útiles.

7. *Locomoción.*—Uno de los grandes beneficios que nos ha traído el creciente progreso de la mecánica ha sido la rapidez y facilidad de la lomoción. Lo que antes habría necesitado días, hoy se cuenta hasta por minutos.

Esta facilidad y multiplicación de los medios de locomoción hace que enfermos y de salud admirable se entrecrucen en la vida, usando reiteradas veces los mismos vehículos y que comarcas salubres reciban frecuentemente individuos que van en busca de sus aires y sus aguas, o de sus paisajes y placeres si se trata de lugares de recreo. En las ciudades mismas la necesidad nos obliga a trasladarnos de un lugar a otro constantemente y para ello usamos vehículos comunes, no siendo raro que el que acaba de servir para trasladar a un enfermo al hospital o a un consultorio médico, sirva inmediatamente a un individuo que aunque vigoroso puede contaminarse por la repetición de esta emergencia.

Los ferrocarriles que transportan diariamente millares de personas entre ellos tuberculosos y que además necesitan un personal crecido que se tuberculiza con extrema frecuencia, y con el cual tenemos que rozarnos y además va transportando el bacilo a largas distancias, ya que ninguna medida se ha tomado para que no sean infectados y mucho menos para que una vez causada esa infección se provea lo conducente a suprimir los males que puede acarrear.

TERRENO.

Lo que dejamos expuesto acerca del contagio muestra claramente que estamos expuestos a la absorción del germen patógeno de la tuberculosis en una proporción alarmante, y más aún, según nos dicen las investigaciones de Dieulafoy, Lermoyez y Strauss, el bacilo se encuentra en individuos sanos.

Nuestro organismo está pues acechado por enemigos de potencia variable, en que la intensidad de sus efectos es proporcional a su número y a su virulencia. "El número de los microbios," dice Bouchard, "tiene su importancia desde el punto de vista de la transmisión y de la gravedad de las enfermedades infecciosas, puesto que aumentando este número se puede vencer la resistencia que un organismo determinado opone a un menor número de agentes infecciosos;" y la misma observación tiene cabida respecto a la virulencia, puesto que un agente o un grupo de agentes infecciosos obrarán con energía proporcional a su vitalidad, a su acción nociva para el organismo, es decir, a su grado de virulencia.

¿Por qué no somos todos tuberculosos? Por que al lado del germen y no sólo en la tuberculosis, sino en toda enfermedad infecto-contagiosa, hay que considerar el terreno; o en otros términos, porque para que la infección tenga lugar se necesita no sólo el bacilo sino el estado receptivo del organismo; o valiéndome de la expresión con que hace sesenta y pico de años explicaba el Profesor Trousseau la manera de obrar de las enfermedades como la tuberculosis: "Sembrad sobre la roca y no obtendréis cosecha; sembrad sobre terreno fértil y la tendréis abundante," y es ese terreno fértil el que prima en la infección tuberculosa, pues como dijimos al hablar de la herencia, la tuberculosis no anida allí donde el organismo le ofrece resistencia.

El organismo humano al estado normal se defiende contra los gérmenes patógenos que tratan de invadirlo; posee medios de defensa y estos medios son los glóbulos blancos, los fagocitos.

De Fleury, quien observa esta lucha al microscopio, nos la describe así:

El glóbulo blanco encuentra en su camino al pequeño bastoncillo, fino, neto, casi elegante, como lo es el bacilo de Koch; se ponen en contacto y el glóbulo blanco absorbe el microbio; se le distingue—intacto, vivaz, en pleno vigor, en plena malignidad por consecuencia, en el interior de la célula fagocitaria.

Bajo la influencia de verdaderos jugos digestivos secretados por el fagocito, el bacilo es roído, alterado, se ahueca aquí, se infla allá, pierde su forma rectilínea, viene a ser una rama nudosa, que se agota, después desaparece digerido, aniquilado por el glóbulo vencedor.

Pero a menudo la batalla es más larga, la victoria más disputada.

Aquí el fagocito no tiene el vigor suficiente para digerir al microbio y al mismo tiempo el microbio no lo tiene tampoco para hacer degenerar la célula, para hacerla perecer. Entonces el microbio, para sustraerse a la acción de los jugos digestivos que le amenazan, se rodea de envolturas estratificadas, que él mismo secreta y que vistas al microscopio semejan a las envolturas concéntricas de un bulbo de cebolla. Ellas le preservan por algún tiempo, mas esta coraza acaba por serle fatal, nociva y muere por inanición.

El glóbulo blanco, por su parte, para acabar de amurallarle, secreta en torno de la coraza microbiana capas de fosfato de cal, que le sirven de tumba; tanto así que la navaja del bacteriólogo se mella en esos tejidos calcáreos cuando quiere hacer cortes para encontrarlos en las preparaciones.

Pero en el hombre el glóbulo blanco es casi siempre el vencido.

Cuando curamos de la tisis, gracias a la eficacia de la higiene, es por mecanismo análogo al de amurallamiento del microbio, de calcificación de las lesiones. El fagocito mata al bacilo y lo encierra con sus venenos en una tumba sólidamente sellada.

Los glóbulos blancos cumplen esta tarea cada vez que tienen la fuerza necesaria, cada vez que nuestro vigor individual está a la altura de su faena.

Pero cuando por esta o aquella circunstancia, nuestro organismo se encuentra debilitado de manera transitoria o permanente, el bacilo vencedor hace degenerar la célula y el mal es dueño del terreno.

Hoy es innegable que el bacilo no triunfa sino de los organismos alterados o decaídos.

Ahora, la resistencia orgánica puede ser vencida y lo es en efecto en proporciones diversas, y de ahí proviene la predisposición mórbida, la aptitud para contraer la enfermedad, el terreno fértil que dice Trousseau.

El terreno, con sus caracteres favorables o desfavorables al desarrollo de la infección, tiene tal importancia, que es de él de que dependen las reacciones clínicas y las diversas localizaciones mórbidas, y es así como se explica también que siguiendo los bacilos la misma vía para penetrar en el organismo—inhalatoria como lo quiere Flugge, intestinal como lo demuestra Calmette—no sea una e igual la intensidad de la infección ni uno solo tampoco el órgano siempre afectado.

El organismo no presenta siempre esa aptitud para recibir y desarrollar las influencias mórbidas, que es lo que constituye el terreno, sino que llega a ello por multitud de causas intensamente depresoras unas veces, reiteradas aunque de intensidad mediocre otras, que vamos a esbozar ligeramente.

Al hablar de la herencia de la tuberculosis, hemos sentado que ella trasmite la decadencia órganica, es decir, el terreno tuberculizable; luego tenemos, en tesis general, que hay una predisposición hereditaria o mejor una predisposición congénita. Pero se puede llegar al mismo estado no sólo sin descender de padres tuberculosos, sino también siendo de progenie de vigorosos.

Las endemias, por su acción debilitante sobre el organismo son causas de predisposición muy marcada, así podemos ver que al paludismo, a la uncinariasis, la disentería amebiana, etc., entre nosotros, preceder o mejor preparar el camino que ha de trillar luego la tuberculosis. Pero entre estas endemias hay una, la social llamada alcoholismo, que es la más temible de todas. No solamente el alcoholismo es una causa poderosa del desarrollo de la tuberculosis en los individuos habituados a este vicio, sino que ejerce una influencia fuera de duda sobre la progenie, dando nacimiento a seres congenitalmente predispuestos, tanto, que dice Jousset, que ser hijo de alcohólico es tanto como ser hijo de tísico y apoya su aserción sobre la encuesta practicada en los países donde impera el alcoholismo.

Desde el año de 1868 presentó Lancereaux un trabajo a la Academia de Medicina de Francia que reposaba sobre la observación de numerosos casos de tisis en alcohólicos; de entonces a la época presente esos trabajos se han multiplicado en todos los países y es un acuerdo general el que reina respecto a este punto de etiología. Lo demuestra claramente que de la mano marchan las luchas anti-tuberculosas y anti-alcohólicas, y que esa influencia nefasta haya hecho decir al Profesor Landouzy que el alcohol prepara el lecho en que anida la tuberculosis, y al Profesor Hayem que la tuberculosis se toma en el mostrador.

Las estadísticas sobre consumo de alcohol y mortalidad por tuberculosis practicadas en Francia establecen que hay una relación constante entre el consumo de alcohol y el desarrollo de la tuberculosis.

En la memoria de 1907 del Henry Phipps Institute, encontramos consignada también esa acción favorable del alcohol en la propagación de la tuberculosis, así como también que los alcohólicos o descendientes de tales son los menos influídos por el tratamiento: el alcohólico permanece en estatu quo o va rápidamente a la muerte.

No citaremos sino para dejar constancia de su error, la creencia de algunos de que tal o cual alcohol sea favorable o preservativo de la tuberculosis. El alcohol, y cuando decimos así, comprendemos todas las bebidas espirituosas cualquiera que sea la materia prima de que se extraigan, obra siempre lo mismo en nuestro organismo; produciendo alcoholismo agudo o crónico y su acción sobre el desarrollo de la tuberculosis, es el mismo, como lo es sobre todas las enfermedades infecto-contagiosas sobre las endemias y epidemias: son los alcohólicos los que pagan más tributos a ellas, como lo demuestran las estadísticas de todos los hospitales y como lo comprobé en el de San Juan de Dios de Bogotá y que consigné en mi tesis inaugural, "Tuberculosis en Colombia."

He aquí los datos estadísticos de Panamá que sobre esta relación entre tuberculosis y alcoholismo; corresponde al año de 1914:

Panamá: mortalidad tuberculosa 229, alochólica 10; Colón mortalidad tuberculosa 86, alcohólica 4; Zona del Canal mortalidad tuberculosa 74, alcohólica 3.

En la ciudad de Panamá hay inscritos hoy 679 lugares de expendio de licores. La producción de alcohol de caña de 33° en toda la República, fué durante el primer semestre de este año de 395,017 litros con 6 decílitros.

El medio social tiene influencia notoria sobre la preparación del terreno para la germinación del bacilo de Koch.

El aire libre, la vida del campo, con su intensidad solar oponen una resistencia verdadera a la tuberculosis. Los arrendatarios, los pescadores, los leñadores, no contraen la enfermedad sino excepcionalmente, dice Gache. En Suiza, la tisis hace una víctima sobre mil habitantes entre los selvicultores y agricultores, y en Italia, sobre mil muertes generales, los pastores y agricultores no tienen sino cuarenta o cincuenta muertes causadas por esta enfermedad.

Entre nosotros, el trabajador de las regiones indemnes de paludismo, de uncinaria americana no hace excepción a la regla citada; pero en nuestros climas ardientes, en las hoyas de nuestro ríos, en nuestras selvas vírgenes, donde el anofeles habita, allí la influencia nefasta del paludismo, aminorando la resistencia orgánica, espera solo que un caso importado se declare para que el contagio se extienda. Cuando las plagas de la producción agrícola obliga a los agricultores habituados a su vida de campo, a buscar en las ciudades el diario sustento, se encuentran reunidas las condiciones para llevar el contagio a los lugares indemnes de tuberculosis; puesto que llegados a la ciudad en malas condiciones de nutrición y produciendo en ellas aglomeración, se tuberculizan bajo las influencias que hemos anotado al hablar del ejército y llevan, al regresar a sus hogares, el grano que ha de germinar en el terreno preparado por la miseria y las endemias.

En las ciudades, donde el excesivo valor del terreno hace caro los alquileres, las condiciones de habitación insalubre se encuentran reunidas, más aún, en aquellas que poco o nada se preocupan por el aprovisionamiento de agua potable y servicio de aseo.

La clase obrera se hacina allí en cuartos que tienen una sola puerta que da acceso a la vía pública o a corredores estrechos, oscuros y húmedos; la cubicación es escasa, a veces el piso húmedo, no están provistas de servicio sanitario aislado, de allí que muchas excreciones sean guardadas por algunas horas para despues verterlas en las alcantarillas, o lo que no es muy raro sobre el suelo en los patios o las vías públicas; la provisión de agua se hace del surtidor más cercano y se mantiene allí sin protección alguna. Al hablar del contagio en la familia hemos notado que en estas viviendas hay promiscuidad de individuos y animales: falta allí, pues, el aire y la luz.

Obran también como causas depresoras predisponiendo el organismo a la tuberculosis al lado de la aglomeración, la miseria, el alcoholismo, la habitación anti-higiénica, la agitación febril de las ciudades, con su vida llena de continuas necesidades, más y más numerosas y apremiantes, la ambición, las contrariedades, las privaciones, etc.

¿La edad tiene influencia alguna sobre la propagación de la tuberculosis?

Algunos autores han citado la pubertad. Bien que ella es una sacudida violenta que sufre el organismo, que se acompaña de fenómenos nerviosos, contra los cuales reacciona aquél según circunstancias que se nos escapan, no puede tener otra influencia que la de todo debilitamiento del organismo Así vemos por lo general, que la pubertad, que pide al organismo un gasto mayor que la infancia, puesto que ella marca el período iniciativo de nuevas funciones y correlativamente el aumento de algunas preexistentes, pasa sin dejar huellas en él; mientras que en otros se acompaña de trastornos que sí las dejarán perennes o transitorias, que indudablemente obran como aliadas poderosas y eficaces del contagio. Pero también es cierto que en estas circunstancias no es ese período de la vida en sí el principal factor, sino el conjunto de atributos anatómicos, químicos y dinámicos inherentes al ser de que nos habla Koch: es el despertar de la heredo-predisposición bajo la influencia del aumento de trabajo del organismo, y no obra la pubertad, en este caso, de manera distinta a cualquier causa extraña en un organismo predispuesto de antemano por los yerros o privaciones de sus antepasados.

"Pubertad y virilidad," dice Peter, "tal es en efecto el período de la vida en que la tisis se presenta con mayor frecuencia y estas nociones hipocráticas son conocidas del vulgo, que no cree en esta enfermedad pasada esa edad, y muchos médicos son vulgo respecto a este punto." No es preciso que sea así. Lo cierto es que el período de la tisis es el de la tuberculización, al cual se llega por predisposición constitucional adquirida o hereditaria; los débiles, los linfáticos, los hijos de tuberculosos, padecen de enfermedades del pecho en la primera o en la segunda parte de estas edades, según la intensidad de la predisposición y de las causas auxiliares. Pero aquellos que habían nacido fuertes y vigorosos, sin tara orgánica alguna, que parecen nacidos para no ser tuberculosos, pueden llegar a serlo a cualquiera edad por la lenta y continua influencia de las causas tuberculigenas y mas aún en la senilidad, que por sí sola constituye una causa de debilitamiento orgánico. Los médicos de los asilos de ancianos conocen este hecho, y Fuller ha podido decir sin exageración que "los tísicos son casi tan numerosos a los 70 como a los 15 años."

El sexo en sí tampoco tiene influencia en la tuberculosis.

En las ciudades en que la mujer trabaja, solo en las labores caseras y en los campos en que no se le exige más que un trabajo proporcionado a sus fuerzas, la tuberculosis es menos frecuente en ella que en el hombre; pero en los centros comerciales y fabriles, en que el salario del hombre no alcanza para el sustento de la familia y la mujer se ve obligada a aportar su contingente de trabajo, la tuberculosis es tan frecuente o más en ella que en el hombre. Esta influencia de la propagación de la tuberculosis en la obrera, es palpable en las ciudades que toman un rápido desarrollo.

Varias causas, que no dependen de su constitución misma, si no del medio en que se agita la mujer en las ciudades populosas es lo que influye en su tuberculización; en efecto, obligada a trabajar en oficios sedentarios, en un aire confinado, muchas veces en aglomeración, con salario exiguo que la obliga a trabajar no sólo durante el

día y la noche sino también en estados, como la preñez y la lactancia, que no le permiten sino una porción de trabajo como uno y le exigen una ración alimenticia y de descanso como dos, su organismo se debilita y es fácil presa del contagio.

Las profesiones no dejan de tener su influencia por el medio en que obligan a permanecer a los que las ejercen. Las estadísticas nos dicen que las enfermeras y los enfermeros, sirvientes de morgue, médicos, etc., que los exponen a un contagio reiterado pagan mayor tributo proporcionalmente a la tuberculosis. Pero lo cierto es que en materia de profesión sucede lo mismo que con las edades, se llega a la tuberculosis por efectos de medio y de contagio: cuando fijadas definitivamente y llevadas a la práctica las medidas profilácticas, las estadísticas de mortalidad tuberculosa por profesiones no presentarán predominancia alguna por ésta o aquélla. En apoyo de nuestro aserto está el que en Bogotá el predominio de la morbilidad y mortalidad tuberculosa correspondende a la clase de oficio doméstico, lo cual le será fácil comprender a todo aquél que conozca aquella ciudad en que las condiciones de vida de su clase pobre se encuentran reunidas todas las condiciones antihigiénicas.

La nutrición es elemento indispensable al mantenimiento de la vida y como tal de defensa del organismo; cuando ella decae bajo el imperio de una acción patológica o de una causa social, el organismo está preparado para la obra devastadora de la tuberculosis.

En una palabra, las condiciones favorables a la evolución del bacilo se encuentran realizadas por todas las causas capaces de producir en el organismo cierto grado de nutrición, sea que obren como causas depresoras, sea que debiliten sus defensas naturales; excesos de toda clase, agotamiento, fatiga, disgustos, preñeces repetidas, traumatismos, intoxicaciones crónicas, etc.

Parte II.—Profilaxis.

La profilaxis de la tuberculosis tiene que dirigirse, como lógicamente se desprende de su etiología, sobre el bacilo para destruirlo y sobre el terreno para preservarlo: una y otra de estas acciones se complementan. Así es que para ser eficaz la lucha anti-tuberculosa no debe descuidar ninguna de estas dos fases del problema.

Destruir el bacilo o ponerlo en condiciones de ser inofensivo, esterilizar la humanidad para el bacilo de Koch, por decirlo así, sería lo ideal, dado que por muy apto que fuese el organismo no existiría la enfermedad si faltase el agente productor. Inconvenientes insuperables en la práctica hacen que la lucha contra el bacilo no haya llegado a desempeñar el papel que la teoría le asigna a primera vista; sin empargo, decía en mi tesis inaugural hace seis años, con el andar del tiempo, vulgarizadas las nociones de higiene, esta lucha será un baluarte poderoso en la defensa de la humanidad contra el flagelo de la tuberculosis, y cuan poco se ha avanzado en nuestros países en este sentido.

En nuestras pequeñas naciones, donde la necesidad de la higiene no ha llamado la atención en absoluto o sólo de una manera mediocre (Panamá y Colón no son obra nuestra), la única fase del problema que puede implantarse por doquiera es profilaxis individual contra el bacilo, enseñando a la humanidad los peligros del contagio y los medios de preservarse de él.

Expongamos algunos de los medios con que contamos para la destrucción del bacilo allí mismo donde se produce.

El bacilo de Koch es muy resistente a la acción de lo agentes físicos, como lo prueban los siguientes experimentos:

Los esputos pulverizados y mezclados con polvos inertes conservan su virulencia después de seis meses: la congelación no los destruye, lo mismo sucede con las temperaturas elevadas; Grancher y Ledoux-Lebard han comprobado que los cultivos de bacilo de Koch, previamente desecados y sometidos al calor seco a 70° durante siete horas, conservan su virulencia; sometidos al calor húmedo a 100° durante tres horas, se debilita su virulencia, pero no se extingue; más aún, Strauss y Gamaleia han demostrado que sometidos los cultivos no sólo a la ebullición repetida, sino al auto-

clave a 115° y 130° durante varias horas (?) e inoculados después, se produce una reacción local un abceso que contiene el bacilo con su reacción micro-química característica. Es pues necesario destruir el bacilo con agentes más prácticos y más energicos como lo son las soluciones antisépticas, cuya acción ha sido bien estudiada.

H. Vincent se consagra en su trabajo titulado "Sobre la desinfección de los esputos tuberculosos," a un estudio sobre el valor comparado de algunos desinfectantes químicos, estudio cuyas conclusiones prácticas son muy interesantes e importantes para el asunto que nos ocupa.

El escollo de la desinfección química reside en el hecho siguiente: que es necesario obrar no sólo sobre el bacilo aislado (desnudo), sino sobre el bacilo protegido, en los esputos, contra el efecto de los antisépticos por un revestimiento formado por sustancias mucosas y albuminoideas. Para la desinfección de los esputos tuberculosos es preciso desechar las sustancias que coagulen rápida y enérgicamente las sustancias albuminoideas.

El mejor de los agentes de desinfección de los esputos sería, evidentemente, aquel que reuna las condiciones siguientes: acción antiséptica absoluta y rápida sobre el bacilo de Koch; que penetre en el producto de la expectoración y se mezcle íntimamente con él; que no sea tóxico; y, en fin, que su valor no sea excesivo.

El autor ha puesto diferentes sustancias desinfectantes durante cierto tiempo, en contacto con los esputos tuberculosos, los ha lavado con agua esterilizada, centrifugado y luego inyectado a los curíes.

De estas investigaciones resulta que se pueden eliminar el aceite pesado de hulla, emulsionado o no, la cal y la potasa, cuya acción no parece satisfactoria. El lysol al 10 por ciento, la soda al mismo título, los hipocloritos y sobre todo el hipoclorito de cal en solución concentrada y diluída luego al 20 por ciento, son los desinfectantes más activos de los esputos tuberculosos.

Por razón de su valor y de ser inodora, la soda al 10 por ciento merece la primacía. En estas condiciones, ella asegura perfectamente, a la temperatura ordinaria, la esterilización de los esputos al cabo de seis horas y aún en menor tiempo; a este título no es caústica, y coloreándola con tintura de tornasol se evitará cualquier error; disuelve y fluidifica los esputos, lo cual impide que se adhieran a las paredes de las escupideras, y por consiguiente facilita considerablemente su limpieza.

Con un desinfectante barato y exento de peligro en su manipulación puesto en cantidad suficiente a disposición del tuberculoso, se daría un gran paso en el sentido de la preservación de sus familiares. Ese desinfectante debe ser acompañado de receptáculos para recibir los esputos una vez salidos de su lugar de producción: las escupideras, de las cuales existen hoy en el comercio distintas clases, desde la de latón barnizado, muy barata, hasta las de porcelana y terracota esmaltadas; lo mismo respecto a su forma que está de acuerdo con el lugar de colocación: de bolsillo, para el piso, y las llamadas colectivas, especies de vasijas como las destinadas a colocar flores y que son muy convenientes para jardines, paseos, corredores, teatros, y en general para todo lugar concurrido.

Con estas dos pequeñas armas bien se puede emprender una campaña de resultados satisfactorios. El uso racional de la escupidera con su solución desinfectante, debe ser vulgarizado lo más posible; para ello es necesaria, la educación, el hábito de no arrojar los esputos fuera de ella, estése o no atacado de tuberculosis. Esta práctica traerá consigo extender la profilaxis a los individuos no sólo atacados de tuberculosis abierta, sino también a aquellos enfermos del pecho, que tienen una afección no tuberculosa, pero que puede llegar a serlo, dados los medios de contagio, de un momento a otro y a los casos no diagnosticados, como sucede en el comienzo de la enfermedad cuando no hay medios para un examen bacteriológico, caso muy frecuente en nuestras ciudades, en las cuales se dice tuberculosis ya cuando los esputos bacilíferos han hecho su obra devastadora.

Debemos propender por todos los medios a nuestro alcance a que la escupidera de bolsillo ocupe el mismo puesto que ha alcanzado el pañuelo, siendo de eficacia mayor el uso de aquella, puesto que el pañuelo es un medio de contagio en los casos, en verdad raros, de tuberculosis naso-faringea. ¿No es mirado como signo de mala edu-

cación no llevar pañuelo para sonarse? Pues hagamos esfuerzos por que otro tanto suceda con la escupidera de bolsillo.

Esta medida profiláctica en extremo laudable, quitaría al uso de la escupidera de bolsillo el inconveniente que tiene de mostrar de modo muy visible al tuberculoso, por lo cual mira con repugnancia su uso y desoye, en detrimento de la salud pública, el consejo o prescripción del médico.

Para triunfar en esta cruzada, es necesario que todo el mundo conozca qué peligro existe en un esputo tuberculoso lanzado libremente al suelo, y que por consecuencia cualquier individuo se sienta con el derecho de llamar la atención al que esputa cerca de él, en vela de su salud y de la de los demás; así como comprender que ese derecho le impone el deber de vigilarse a sí mismo para no incurrir en la misma falta que corrige a otro. Por otra parte, el médico debe advertir al tuberculoso que no debe participar libremente de la vida en comunidad, si no sigue la regla de usar su receptáculo para esputos, a lo cual se mostrará sumiso si al mismo tiempo se le hace conocer que las primeras víctimas del hábito deplorable de escupir en los pisos son sus allegados. Indefectiblemente, como dice P. Brouardel, el día en que haya desaparecido la desagradable y peligrosa costumbre de escupir sobre el suelo, la tuberculosis decrecerá rápidamente.

Nada debe ahorrarse y todos los medios son buenos para llegar a este fin. Hoy vemos por doquiera los avisos de "Prohíbese escupir sobre el piso," lo que nos demuestra que el consejo del Dr. Bourland, en su relación a la Asociación Médica Americana, ha dado sus resultados. Ese aviso diseminado por doquiera ha hecho sus progresos ya, inculcando en el público el peligro del esputo. Pero es preciso completarlo poniendo al lado del aviso la escupidera para aquellos que, por sufrir una afección de las vías aéreas, se ven en la necesidad de esputar en los lugares concurridos; además, ya es tiempo que la prohibición sea seguida de corrección: los agentes encargados de vigilar la seguridad pública, quedan impasibles ante un individuo que arroja sus esputos sobre la vía pública; a ese se le debe instruir sobre lo que eso significa e imponerles el deber de vigilar porque la prohibición no sea letra muerta, e imponer penas a los que así atentan contra la salud pública. El día que se castigue con multas a los que cometan esta falta, no habrá más infractores de esa medida sanitaria.

Las asociaciones de obreros, el periodismo, las conferencias públicas, prestarán una ayuda eficaz a esta profilaxis individual. Y los gobiernos por su parte deben hacer obligatoria entre el personal docente la enseñanza anti-tuberculosa, para que ellos a su vez la hagan extensiva a los niños, ya que ellos van a ser los hombres de mañana.

Eso en cuanto a lo que debe hacer el individuo aisladamente, a la profilaxis individual.

Ahora, colectivamente, debemos principiar por la desinfección obligatoria y reiterada de las habitaciones de los tuberculosos, sobre todo en la actualidad, en que no promulgadas aún las enseñanzas arriba indicadas, la habitación en común con estos enfermos es muy peligrosa. Incluída como está la tuberculosis en el número de las enfermedades de declaración obligatoria, ésta debe ser seguida de la desinfección del domicilio del enfermo periódicamente.

Incluir entre las medidas sanitarias la desinfección de las casas de alquiler, antes de ser reocupadas cuando no se conozca el estado patológico del inquilino saliente. Los escrúpulos que esta medida traerá consigo al principio, irán desapareciendo con el hábito y con la convicción racional de que el servicio sanitario deja a su salida de una casa, la convicción de que es habitable sin temor alguno.

La declaración de los casos de tuberculosis en su principio no llenará completamente su objeto, ya sea el médico de cabecera, la familia, los dueños de hoteles, casas de asistencia, u otros análogos los encargados de hacerla, debido a la aparente repudiación que el sistema tiene de atraer sobre el enfermo la atención pública; pero la propaganda activa por medio de conferencias públicas, de lecciones objetivas por

medio de cuadros murales y la voz del médico, en cada caso particular, llevará a los ánimos la convicción de la necesidad de él y la del peligro que, para la familia, las agrupaciones industriales, las ciudades y los países en general, trae su omisión. Así llegará el día en que el enfermo mismo, por condiciones de interés personal bien entendido, solicite la desinfección de manera imperiosa, como sucede hoy en Panamá con la difteria, la escarlatina, etc.

Para que esta desinfección llene todo su cometido, se necesita que todos los casos de tuberculosis sean conocidos de la oficina de sanidad y sobre todo las tuberculosis al principio. Ninguna institución puede llenar este cometido como los dispensarios antituberculosos y entre estos el dispensario tipo Calmette, que tiene la ventaja de controlar los casos que van en busca de auxilio y de despistar casos que no se habrían presentado sino muy tarde y que además va inculcando en las masas la confianza y la necesidad de recurrir allí apenas se siente algún síntoma de enfermedad del pecho. Estos dispensarios, que podremos establecer como una rama de nuestros hospitales de caridad, dotados de personal competente, con laboratorio bacteriológico para exámenes de esputos, se encargaría de indicar los lugares que necesitan de la desinfección.

No está de más, dada la importancia de estos dispensarios, dar aquí una idea completa de lo que son. Dice Calmette:

Pienso que en lugar de esperar que el obrero tuberculoso venga a consultar al médico ya obligado a la suspensión de trabajo por la enfermedad, debe erigirse en principio la necesidad de ir a él y de prestarle asistencia, antes de que se aperciba de que está gravemente atacado. Quisiera que fuese posible despistar en el enfermo la tuberculosis muy al principio de su evolución y que se esforzase también en darle los consejos y cuidados que puedan serle útiles para conservarlo el mayor tiempo entre su medio y su familia.

He aquí como es posible organizar prácticamente la lucha contra la tuberculosis en la clase obrera:

Se crearía primero en cada ciudad un número suficiente de dispensarios de barrio para que cada uno de ellos pueda fácilmente atender a una circunscripción determinada.

El papel de los dispensarios consistiría:

1°. Ponerse en relación con todos los jefes o capataces de fábricas y talleres y con todos los establecimientos que ocupen obreros protegidos por la ley de aseguros contra accidentes.

2°. Buscar, gracias a los datos suministrados por los jefes o capataces de las fábricas o talleres, los obreros sospechosos de tuberculosis; atraerlos al dispensario para darles, tan a menudo como sea necesario, consultas gratuitas, consejos para su familia; distribuirles cuando estén obligados a suspender su trabajo, socorros en dinero o alimentos, vestidos, medicinas, libros.

3c. El dispensario de cada circunscripción deberá matricular todos los enfermos de su dependencia, hacerlos visitar frecuentemente a domicilio, procurarles ocupaciones o trabajos en relación con sus aptitudes y con su estado de salud; hacer desinfectar sus alojamientos toda vez que esta operación pueda ser útil; suministrarles las escupideras higiénicas; indicarles como se deben destruir los esputos; esterilizar sus ropas; dar en una palabra, todas las instrucciones necesarias para asegurar las mejores condiciones higiénicas en su domicilio al tuberculoso y preservar del contagio a aquellos que lo rodean y de los cuales no puede ni quiere separarse.

Querría que cada dispensario fuese dirigido por un médico especialmente instruído en vista de las funciones que debe llenar y que haya hecho un curso suficiente en los laboratorios bacteriológicos, para tener competencia en los exámenes regulares de esputos que haga a los enfermos y controlar así la eficacia de las desinfecciones que haya prescrito.

Está por de más decir que los dispensarios estarán provistos de los instrumentos y útiles necesarios para la observación rigurosa de los enfermos (microscopio, báscula, dinamómetro, etc.) y que cada obrero matriculado, al pasar de una circunscripción a otra, fuese provisto de su expediente clínico.

La administración de los dispensarios sería, en mi opinión, ventajosamente confiada a las municipalidades, a lo menos en las grandes ciudades, con un control del Estado y bajo la reserva de que una ley hiciera su creación obligatoria en todas las aglomeraciones obreras de alguna importancia.

Los gastos de instalación serían evidentemente poco considerables, pero su mantenimiento exigiría sacrificios pecuniarios importantes, en razón sobre todo a subvenir

a las necesidades de las familias de los obreros enfermos. Según mis cálculos aproximativos, cada obrero cuidado o vigilado por el dispensario, comprendiendo en ello los socorros distribuídos a domicilio, costaría en término medio 3 francos por día de invalidez.

En Panamá, y en los países similares, la creación de estos dispensarios se impone, ya sea aislados o, como lo dije anteriormente, dependientes de los hospitales de caridad ya establecidos. En cuanto a sus fondos, ya que poco o nada puede esperarse entre nosotros de la iniciativa particular, tienen que emanar del tesoro nacional o de los municipios, los cuales pueden establecer un gravamen o contribución especial sobre los artículos de lujo y al mismo tiempo un seguro obligatorio a los empleados públicos, contra la tuberculosis.

Ahora con el fin de hacer llegar sin desconfianza a todos los enfermos, esos dispensarios deben ser denominados "Dispensario para curar las enfermedades del pulmón" como lo propone P. Brouardel.

Debo consignar aquí el número de tuberculosos existentes hoy en la ciudad de Panamá y en la República para que se tenga base para un cálculo aproximativo. Siguiendo la proporción que da "La comisión permanente contra la tuberculosis" en Madrid para investigar el número de tuberculosos existentes por el número de defunciones causadas por esta enfermedad (cinco enfermos para cada defunción), tenemos que la ciudad de Panamá con 229 defunciones en el año de 1914, tendrá 1,145 enfermos tuberculosos y que la República entera con 504 defunciones, tendrá 2,520.

A los hospitales generales de hoy llegan tuberculosos en número no despreciable y esta circumstancia debe aprovecharse para controlar los focos de donde provienen y proceder a su desinfección.

Al hablar del contagio en los hospitales, dijimos que son un contra sentido los policlínicos para alojar a los tuberculosos, de aquí que se imponga ya sea la creación de establecimientos adecuados, ya, como medida paliativa, la instalación de salas especiales, con personal competente, instruído profilácticamente para que a su vez instruya a los enfermos y a su salida dejen de ser un peligro para sus semejantes: que esas salas sean un medio de vulgarización y no asilos que el enfermo solicita cuando ya sus recursos no le permiten hacer otra cosa.

Los cuerpos que dependen del gobierno, ejército, gendarmería, policía, deben recibir instrucción antituberculosa. Así será fácil la cruzada por la profilaxis individual.

Indicadas las medidas para hacer inofensivo el bacilo de Koch, hasta donde sea posible, y que llevadas a la práctica el tuberculoso dejará de ser un peligro para sus semejantes, resta indicar los medios para evitar la receptividad del organismo, lo cual complementará los buenos frutos obtenidos por aquellas. Hemos anotado que las causas principales que hacen el organismo receptivo, son: el alcoholismo, la habitación insalubre, excesos de toda naturaleza, mala o deficiente alimentación y las habitaciones insalubres.

El alcoholismo y la tuberculosis, su compañera, van de la mano diezmando la humanidad y contribuyendo a la decrepitud de la raza. De la comprobación de los efectos de aquél, ha surgido la lucha anti-alcohólica que se propaga por el mundo bajo auspicios venerables.

El Profesor Debove, en su discurso ante La Liga Nacional contra el Alcoholismo y La Unión Francesa Anti-alcohólica en París, se expresó así:

El alcohol puebla nuestros hospitales, nuestras cárceles, nuestros manicomios. Despuebla nuestro país merced al aumento de la mortalidad, a la disminución de los nacimientos y a la procreación de hijos que llevan el estigma de su origen. Su acción maléfica se ejerce de un modo desigual en nuestros departamentos. Es fácil conocer cuales son los más atacados: los que registran menos nacimientos y más criminales, los que tienen más hombres rechazados para el servicio militar. Si siguen así las cosas, desaparecerá nuestra patria. Sería inútil mantener un ejército si en el interior tene-

mos un enemigo que nos destruye con más seguridad de lo que podría hacerlo una potencia militar. Sería inútil intentar esfuerzo alguno para el mejoramiento material y moral de un pueblo, cuyos días de existencia estuviesen contados.

Meditando las palabras del ilustre profesor francés, encontramos en ellas consignada, al par que los inmensos perjuicios del alcoholismo, la imperiosa necesidad de emprender la lucha contra él, en el mundo entero, porque las enseñanzas que encierran no son tan sólo para la Francia, ellas traspasan los límites de esa nación para hacerse universales.

Hurguemos en ese estercolero social—el alcoholismo—y encontraremos cuánta inmundicia, al par que cuántos reproches para los que miran impasibles los males evitables. Y cuánta execración para los que convierten el envenenamiento del organismo, la decrepitud de la raza, en comercio lícito.

La lucha antialcohólica reviste dos fases: la acción oficial y la iniciativa privada. En los países en que esta lucha se ha instalado, la primera de sus fases ha limitado su acción a imponer gravámenes al alcohol destilado, dejando de este modo desarrollarse las bebidas fermentadas que producen el mismo mal que el anterior. Entre nosotros se ha hecho lo mismo, creyendo que el aumento del valor de la primera bebida detendría el abuso de este veneno, y hemos observado que ha aumentado la producción de cervezas, cuyo consumo lleva al mismo fin: la embriaguez y el deterioro del organismo. En algunos Estados de la América del Norte el consumo de bebidas espirituosas está terminantemente prohibido. Esta medida nos parece la más eficaz. Más ya que quizás éta no puede llevarse a efecto, creemos que la acción oficial prestaría gran apoyo a esta obra necesaria, gravando fuertemente las bebidas destiladas y fermentadas (cervezas, licores), a fin de acabar con la industria que deprime e idiotiza a la humanidad y desplueba las naciones. Las municipales deben gravar igualmente las cantinas y demás lugares de expendio de estas bebidas, dedicando su producto a la salubridad pública.

La segunda es más eficaz, y para cumplirla debidamente debe ser múltiple en su acción: debe principiar en el hogar, proseguirse en la escuela, donde al par que la educación, se enseñen las nociones de higiene individual y el temor al peligro alcohólico; las escuelas nocturnas para artesanos llevarían este cometido fácilmente y producirían benéficos resultados; combatidas allí las nociones erróneas del alcohol como alimento de ahorro, como ración complementaria de la vida, se prepara al ciudadano temperante de mañana; completar estas nociones con conferencias públicas; fomentar las sociedades temperantes iniciadas ya en muchas partes del mundo; por medios de cuadros murales, profusamente repartidos, que sean una lección objetiva de los males que trae consigo el alcohol; del réclame anti-alcohólico, colocado al lado del réclame alcohólico, al cual han propendido de manera eficaz los certificados expedidos a las bebidas llamadas higiénicas.

Las sociedades de obreros y religiosas pueden prestar un valioso contingente a esta obra, haciendo figurar en sus estatutos la prohibición del alcohol y organizando conferencias para que sus miembros lleven al espíritu de los asociados la razón de esa medida, tal como lo hacen sus conferencistas llevando la palabra evangélica, predicando la salvación de las almas; así su servicio sería para Dios y la Patria: al primero devolviendo al rebaño las ovejas descarriadas que lavan su pecado en la fuente del arrepentimiento; a la segunda, devolviendo al trabajo, a la industria y arrebatando a la miseria, a la locura, al crimen, multitud de descarriados, que son hoy una carga para sus semejantes y procreadores de seres de miseria moral y material, que mañana no podrán contarse como unidades al servicio de ella.

La habitación anti-higiénica, de cuyo papel etiológico en la enfermedad a que nos referimos ya nos hemos ocupado, cuenta también para su destrucción con la acción oficial y la iniciativa privada.

Las municipalidades, por medio de su inspección técnica de higiene, deben hacer desinfectar las contaminadas, contribuir al mejoramiento de la habitación del obrero,

y, punto importantísimo para nosotros, que contamos con ciudades que inician su desarrollo, impedir que se construyan edificios sin la inspección higiénica, para lo cual deben ordenar que no se puedan edificar dichas construcciones sin que la municipalidad apruebe los planos correspondientes, más si se trata de pasajes o edificios análogos para arrendar. De esta manera se previene, tarea más fácil y eficaz que corregir.

La iniciativa privada ha llevado a Inglaterra a ocupar el primer puesto entre las naciones mejor organizadas para la lucha contra la tuberculosis y también la que ha obtenido mejores resultados. Cerca de 60,000,000 de pesos han invertido los capitalistas de Londres en la construcción de casas higiénicas a bajo precio para obreros, que les producen un interés módico de su capital y al mismo tiempo han contribuído poderosamente a mejorar las condiciones sanitarias de esa ciudad.

La habitación higiénica a bajo precio hará desaparecer el tugurio y dará una enseñanza prática a los constructores de habitaciones para arrendar, que solo se han preocupado hasta hoy del tanto por ciento, a más de que, inspeccionadas debidamente, enseñarán el aseo al pueblo; su bajo precio dará un aumento a la ración de nutrición y por él tendrá ella una doble y benéfica faz en el mantenimiento normal de la resistencia orgánica, es decir, en conservar la inmunidad contra los gérmenes de las enfermadades infecto-contagiosas.

Esta obra debe ser acogida con beneplácito por los capitalistas y al ayudarla y proseguirla prestarán un precioso contingente al servicio de la Patria.

Al par que la lucha anti-alcohólica y la habitación higiénica, se ha puesto en práctica la fundación y explotación de restaurantes para obreros, cercanos a los focos industriales y fabriles. en Buenos Aires, debido a la iniciativa de la Sra. de Coni, uno de los cerebros femeninos más culminantes de la América, quien ha unido de manera gloriosa su nombre a la lucha anti-tuberculosa de su patria.

El pensamiento así expresado dice el doctor Gache en contestación al proyecto de la Sra. de Coni, señala por ahora el primer paso en el sentido de mejorar fundamentalmente el régimen alimenticio del trabajador para hacerle fuerte y colocarle en condiciones de resistir mejor las influencias nocivas, alejándole al mismo tiempo de la taberna y de los sitios peligrosos.

El fomento de esta obra tendría la inconmensurable ventaja de suprimir o a lo menos de restringir el restaurante-licorería, donde el jornalero consume la mayor parte de su salario en la bebida, y alimentándose por ello muy deficientemente.

La influencia nociva de los excesos físicos se nota también casi exclusivamente en la clase obrera sobre todo en la mujer, que lleva sobre sí el peso de la escasez de su salario y en ocasiones trabaja de día y de moche, a pesar de la maternidad y la lactancia.

Los más expuestos al deterioro de su salud por los excesos físicos son la mujer y el niño obreros, como muy bien nos lo indica la Sra. de Coni, de la Argentina: en aquélla, por las razones anotadas; en éste, porque apenas llegado al uso de razón necesita ganarse la vida, en ocasiones en oficios fuertes y con el mismo horario de trabajo que el adulto, lo cual impide el desarrollo normal de su organismo.

Las leyes de protección del obrero se encuentran en vigencia en la totalidad de las ciudades europeas.

La obrera que aun estando embarazada necesita trabajar, dará al mundo hijos raquíticos y predispuestos para la tuberculosis; si lacta en las mismas condiciones, su hijo abandonado en el tugurio no alcanza generalmente a la adolescencia, víctima del mismo mal o de alguna otra enfermedad infecto-contagiosa. Estudiadas las causas de la crecida mortalidad infantil en los centros fabriles, se ha llegado a la fundación de asociaciones para preservar al hijo intra y extra-uterino de la obrera; las primeras, por medio de casas de maternidad donde ella permanecerá desde cierto tiempo del embarazo hasta después del puerperio, con solo pagar una pequeña cuota de su salario; la segunda, por medio de casas niñeras, donde se recibe y se cuida el hijo de la obrera mientras que ella está en el taller.

Tuberculosis y matrimonio.—El hombre tuberculoso no debe casarse, no solamente porque agravaría su estado de salud por los excesos y fatigas que impone el primer período del matrimonio; no sólo porque contaminaría a su esposa, sino porque lo que es más grave aún, procrearía hijos débiles, raquíticos, que, si no están tuberculosos desde su nacimiento, quedarán en circunstancias favorables para, tarde o temprano, ser presa de la terrible enfermedad y esparcir a su turno el contagio.

En cuanto a los niños hijos de mujer tuberculosa, son aún más raquíticos y están más predispuestos a la enfermedad que los de hombre tuberculoso y mujer indemne. Es necesario, dice Peter, que la tuberculosa no se case, y si es casada, que no tenga hijos: son tan inútiles a la sociedad como nocivos a su madre; son niños cuya vida es un problema no resuelto aún.

Para toda mujer la preñez es una fatiga, y la tuberculosis la exagera. La enfermedad queda estacionaria hasta el parto; algunas veces la enferma se siente mejor; pero después del parto, la enfermedad, como si hubiese recibido un empuje poderoso, toma una marcha fulminante y la muerte no se hace esperar.

Así pues nos dice el Profesor Tarnier, es preciso evitar la preñez en una mujer tísica. "En caso de presentarse, el partero cuya intervención es ineludible, tiene que someter la enferma al régimen higieno-dietético y en ocasiones provocar el aborto, que practicado en tiempo puede salvar a la enferma. Estas consideraciones bastan para comprender la necesidad de aplicar el aforismo de Tarnier."

La lactancia es prohibida por la ley francesa, que dice: "toda mujer tuberculosa o sospechosa de estarlo no debe lactar. Hay peligro en ello no sólo para ella, ya que la lactancia, por las fatigas que trae consigo, agravará su estado, sino que corre peligro la salud y la vida de su niño."

Para la tuberculosa, la ley de Peter es de aplicación rigurosa: "soltera, no debe casarse; casada, no debe tener hijos, y si los tiene, no debe lactarlos."

Independientemente de los peligros que trae consigo el matrimonio entre tuberculosos: para el hombre, las relaciones sexuales repetidas; para la mujer, la preñez; para uno y otro, la hemoptisis inminentes; existe el peligro de la contaminación a un cónyuge sano por el otro enfermo. En realidad, los besos, la vida en común, son entre nosotros causas casi fatales de contagio descuidadas, por no ser conocidas las reglas que pueden, si no evitarlo seguramente, a lo menos alejarlo. Y este contagio, según lo ha observado Teutsch, no sólo se observa entre individuos que viven continuamente unidos, sino también entre aquellos que tienen relaciones espaciadas o casuales.

Como regla general, resumiendo, los tuberculosos deben tener relaciones sexuales tan cortas y alejadas como sea posible; para evitar el contagio, la boca debe mantenerse en estado de aseo perfecto y vigilar con cuidado los bigotes y la barba; lo mejor sería efeitarse con frecuencia; seguir estrictamente las reglas de la profilaxis individual.

Los enfermos cébiles están condenados a no casarse nunca? No, pero es preciso esperar que el tratamiento haya producido un resultado feliz y que las apariencias de curación se mantengan durante varios años. He aquí como resuelve la cuestión Daremberg.

Cuando el tuberculoso o la tuberculosa están bien curados, desde hace cinco o seis años, pueden casarse si tienen recursos suficientes para no estar obligados a trabajar excesivamente para el sustento de la familia. No se deberá olvidar que los niños hijos de antiguos tísicos son delicados y que deben tener no solamente una buena alimentación, sino que deben vivir al aire libre.

Para llegar a este fin curativo, a este límite fijado por Daremberg, la necesidad de un diagnóstico precoz, elementario sin el cual el tratamiento no alcanza resultado satisfactorio, se impone. Este diagnóstico precoz comprende el período llamado por el Profesor Grancher "de germinación o pretuberculoso."

APÉNDICE.

Expuestas las medidas preventivas de la tuberculosis, debemos indicar, para completar este estudio, que debe hacerse con los tuberculosos existentes, ya que no debe mirárseles como parias, máxime cuando su crecido número obedece a la incuria en que hemos vivido. Hay que tener en cuenta que al mejorar su situación, al colocarlos en mejores condiciones nos defendemos todos del flagelo que nos amenaza cada día más y más: utilidad común de la cual debemos imponer a todos, para que nadie escatime su grano de arena a la obra anti-tuberculosa.

Las medidas preventivas nos llevarán a disminuir o, sería el ideal, suprimir los tuberculosos del porvenir. Pero es necesario tratar a los enfermos, tanto más cuanto que las estadísticas nos dicen que la enfermedad es curable y en muchas ocasiones curable espontáneamente como se ha comprobado millares de veces en las autopsias.

Los enfermos que no tienen recursos para ser tratados en sus domicilios debidamente, y aquellos para quienes el dispensario no puede servir, por lo avanzada de su enfermedad o durante los ataques agudos, deben ser hospitalizados racionalmente en espera de una mejoría o de una curación radical. Estos hospitales son los sanatorios, que deben ser instalados por el estado o las municipalidades, como lo son los hospitales de caridad, sin perjuicio de que los haya particulares para las clases pudientes.

Lo difícil de estos establecimientos es su mantenimiento, debido a su costo, pero esto puede allanarse en parte con el establecimiento del seguro obligatorio del obrero y del empleado civil, lo cual ayudará al Estado a sobrellevar la carga que su creación le impone.

Este seguro es más fácil de establecer en los cuerpos como el ejército, marina, policía, etc., como en los llamados Montepíos militares fundados con fines parecidos o con el de asegurarles algún dinero a su salida de servicio.

Los niños tuberculosos no deben concurrir a las escuelas, comunes, pero se pueden establecer escuelas especiales donde al par que desarrollan sus funciones psíquicas encuentren medio de reponer su salud; de allí volverán muchos sanos y vigorosos a ser útiles a su patria. Estos establecimientos funcionan hoy en varias partes del mundo con el nombre de Colonias agrícolas para niños tuberculosos.

En cuanto a los niños no tuberculosos, pero hijos de tales, que viviendo al lado de ellos llegarán a serlo indudablemente debido al estado receptivo de su organismo, se impone el tomar alguna medida para evitarles la enfermedad. Entre las que se han ideado para ello, nos parece la más práctica y la más facil de llevar a cabo, la de la obra de preservación de la tuberculosis por el método del Profesor Grancher: He aquí como lo describe De Fleury.

Su objeto preciso, es sustraer al niño, ileso de la enfermedad, del medio tuberculoso en que crece, expuesto día y noche al contagio. Está hoy demostrado que la tisis no es hereditaria, pero sí muy contagiosa, y todo el mundo comprenderá la importancia fundamental de esta noción actualmente indiscutible.

El médico de una oficina de beneficiencia o uno de esos investigadores de la tuberculosis, como los ha imaginado el Profesor Calmette para sus dispensarios, avisaría a los agentes de la obra de preservación que existen, en tal o cual casa insalubre de la ciudad, por ejemplo, dos niños aún sanos cuyos padres están enfermos de tuberculosis. Un médico inspector se traslada a la casa, comprueba que los niños están completamente ilesos y que no podrán, pues, contaminar el medio a donde van a ser transplantados. La obra propone entonces a los padres servirles de intermediaria para colocar a sus hijos en el campo, en una familia de labradores perfectamente sanos. Allí crecerá el niño al aire libre, lejos de todo contagio, suficientemente alimentado, y quedará pronto vencida su debilidad natural. Al mismo tiempo se aligeran los cargos del padre de familia y el trabajo de la madre.

Queda bien establecido que nunca se obligará a los padres a separarse de sus hijos. Conviene que se impongan voluntariamente este sacrificio necesario y que la obra sólo le sirva de intermediaria. Además los padres estarán obligados a pagar por su hijo una cantidad ínfima, dos o tres francos por año, que se les adelantarán si es necesario, para indicar que no abandonan a su hijo, que no se desinteresan y que conservan contacto con él.

La obra concebida por el Dr. Grancher lleva estampado el sello de su espíritu tan neto, tan juicioso y tan perfectamente clarividente. Este maestro, que consagró más de la mitad de su vida al estudio de la tuberculosis, ha contribuído, más que nadie, a demostrar su unidad, ha descrito los signos que permiten hacer el diagnóstico precoz; este profesor de clínica de enfermedades de la infancia, a quien no han faltado las ocasiones de conmoverse ante los sufrimientos de los pequeñuelos; este bacteriólogo, cuyo nombre vivirá siempre como el de uno de los primeros y más eminentes discípulos de Pasteur; este hombre estaba particularmente señalado para concebir y organizar semejante obra de preservación que, en cualquier sitio donde funcione, pondrá fin a la propagación y detendrá la diseminación del más atroz de los azotes, salvando a la infancia, aliviando a la familia atacada, de todos los gastos y pesares que cuesta la obligación de criar a unos infelices que la enfermedad y la miseria hacen sentir haber echado al mundo.

Se recogen los niños entre cinco y trece años y permanecen en el campo el tiempo necesario para el pleno desarrollo de sus fuerzas y el saneamiento de la casa paterna; y su destierro, suavizado por las frecuentes visitas de los inspectores de la obra, es fecundo en resultados fértiles para ellos mismos, para sus padres y para la sociedad.

Toda obra de beneficiencia, de preservación y de asistencia, ha dicho el Profesor Grancher, lo mismo si vive de la caridad pública o con el dinero del Estado, tiene por deber hacer el mayor bien posible con el menor gasto. Más que ninguna otra, la obra de preservación de la infancia contra la tuberculosis, parece llenar estas dos condiciones.

Hace ya tres años que se fundó. Algunas cifras van a decirnos lo que ha realizado desde entonces.

En 1904 aseguró la salvación de 27 niños amenazados de tuberculosis; en 1905, el número de sus pupilos se elevó a 50, y en 1906, a 223, repartidos entre 12 hogares; cada uno de estos hogares está colocado bajo la vigilancia de un médico de la comarca, afiliado a la obra.

Reconocida de utilidad pública, la obra del Profesor Grancher recibe ahora del Estado 50,000 francos, la ciudad de París le concede 18,000 y el consejo general del Sena 7,000 por año.

Los adherentes, fundadores de pensiones o plazas, bienhechoras, donantes, etc., son anualmente 1,048.

El valor de cada niño se ha calculado en 200 francos anuales, y esto hasta los 10 o 12 años, pues de dicha edad en adelante ya no costará, nada, porque su trabajo, de acuerdo con su estado de salud, dará sus gastos.

Otras ciudades de Francia han seguido el ejemplo, y en todas ha dado los más halagüeños resultados, y de Fleury nos dice que—

Basta con que continúe este movimiento para que dentro de pocos años estén en toda la Francia los hijos de tuberculosos al abrigo de un mal que no podía dejar de alcanzarlos. Se habrá salvado la semilla, como decía Pasteur, y habrá dado Francia al mundo una incomparable lección de discernimiento, de sabiduría y de economía, en materia de lucha anti-tuberculosa.

CONCLUSIONES.

La etiología de la tuberculosis se basa sobre dos puntos capitales: el bacilo de Koch, agente específico de dicha enefermedad, y el organismo en que éste se desarrolla.

Antiguamente era dogma la herencia de la enfermedad. Hoy, merced a los progresos de las ciencias biológica y fisiólogica y a su ayudante la bacteriología, ésta ha perdido su predominio y nosotros concluímos que excepcionalmente se hereda la tuberculosis, rara vez es congenital por contagio intra-uterino, y que la herencia no interviene sino predisponiendo el organismo a ella, es decir, que los hijos de tuberculosos nacen débiles y esto los hace receptivos.

La propagación de la enfermedad en el mundo se debe al contagio.

El bacilo de Koch, agente del contagio, existe, por millares en los esputos de los tísicos. Los esputos, tanto al estado fresco acabados de expulsar, como seco y reducidos a polvo, son la causa primordial de la extensión que ha tomado la enfermedad. Fresco, puede contaminar las manos, libros, objetos de uso común, etc., ser llevado por las moscas sobre nuestros alimentos y de ahí pasar a nuestro organismo por el tubo digestivo. Seco se pulveriza y esos polvos pueden penetrar en nuestro organismo, depositándose sobre los mismos objetos enumerados y penetrar por la misma vía o en casos excepcionales con el aire inspirado.

Los animales tuberculosos y que sirven a nuestra alimentación pueden también llevar su bacilo a nuestro organismo y producirnos la enfermedad; gracias a la inspección de carnes, éstas presentan un peligro casi depreciable; no así con la leche que se contamina fácilmente por el esputo humano.

La miseria, toda causa que debilite el organismo, lo hace receptivo para la tuberculosis y en muy alto grado, el alcoholismo, llamado por eso el gran tisiógeno.

La habitación en un cuarto o casa, con gran número de personas y con animales, sin servicio sanitario, en desaseo, entra en el número de las causas más poderosas de debilitamiento del organismo y por ende de la propagación de la enfermedad.

En los medios colectivos en que estas condiciones se encuentran reunidas, los contactos entre los individuos son frecuentes y las ocasiones para el contagio son tanto más de temer cuanto mayor sea el número de los cohabitantes. Sucede así en las casas de alquiler por cuartos, los talleres o fábricas, los asilos, establecimientos de castigo, los hoteles, el ejército, la marina, los navíos, los trenes, escuelas, etc., y en algunos como los hospitales policlínicos de caridad que se encuentran habitados por tuberculosos en número no despreciable.

En todas partes donde el hombre se reune para su trabajo o sus placeres, se puede contraer la enfermedad si entre los reunidos existen tuberculosos que no toman precauciones con sus esputos.

La tuberculosis es una enfermedad que se propaga no tanto por ser ella inminentemente contagiosa, sino por la incuria en que vivimos y por la arraigada idea de ocultar al tuberculoso su estado y lo que es para los demás, si no se ajusta a las prescripciones de una higiene individual al parecer rigurosa, pero benéfica en extremo para los seres que ama y para quienes desea los mayores bienes posibles.

La tuberculosis es pues una enfermedad evitable y el medio más eficaz y fácil para ello es la higiene individual, cuidando al mismo tiempo de no esparcir los esputos sobre los pisos, ya sea de la habitación o de las vías públicas, con mayor razón en la proximidad de las sustancias que sirven a nuestra alimentación. Guerra al esputo debe ser el lema de la cruzada antituberculosa.

Las municipalidades no deben mostrarse indiferentes a este movimiento preventivo, dictando disposiciones que hagan efectiva la prohibición de escupir en los lugares públicos y proveer sus edificios de escupideras adecuadas y suficientes.

Estas secundadas por el Estado deben contribuir a la fomentación del servicio de desinfección y de los dispensarios; al mejoramiento de los hospitales policlínicos para evitar que sean un medio de propagación; creando y manteniendo los sanatorios para alojar a los tuberculosos en períodos curativos; preservando a la infancia de la enfermedad, contribuyendo a que se levanten fuera del foco tuberculígeno en que han nacido.

Las asociaciones de obreros; las grandes fábricas y talleres; las asociaciones de comercio; los empleados civiles y militares, deben establecer el seguro obligatorio contra la tisis. Así se hace obra de prevención y se pueden ahorrar muchas penalidades en lo porvenir.

En estas agrupaciones humanas como en las escuelas debe llevarse a cabo la instrucción antituberculosa para que sus miembros, comprendiendo la necesidad de ella la practiquen en sus hogares y por doquiera.

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LA TUBERCULOSIS EN BOLIVIA; SU ETIOLOGÍA Y PROFILAXIA.

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El título del presente estudio, parece indicar que abarca todo lo que se refiere a la tuberculosis y sus caracteres especiales, en las distintas zonas de la República, pero como un tema tan vasto requeriría más tiempo que el que actualmente dispongo, para su correcto desarrollo, sólo me ocuparé por el momento de la tuberculosis en la región del altiplano y muy especialmente en los departamentos de La Paz y Oruro.

La tuberculosis, cual hacen notar con razón la mayor parte de los autores, es conocida desde la más remota antigüedad, confundida al principio con todas las enfermedades que determinaban intenso desgaste orgánico, fué poco a poco mejor caracterizada, hasta que las investigaciones de Peter, Bonet, Morton, Sauvages y finalmente Laenec, la hicieron conocer en su integridad clínica, estableciendo emás la anatomía patológica de la afección.

Lejos se encuentra ya de nuestra época, la de las ardientes discusiones de la escuela dualista con Virchow a la cabeza y la unicista cuyo paladín fué Villemín. Sabido es que las experiencias de inoculación hechas por este sabio, el 5 de diciembre de 1865 y el descubrimiento del bacilo de Koch, el 24 de marzo de 1882, vinieron a sentar sobre bases inconmovibles la absoluta unidad de la tuberculosis, cuyas modalidades clínicas por muchas y muy variadas que fueran, siempre estarán en último término producidas por el mismo bacilo.

El descubrimiento del agente productor de la enfermedad, fué uniformemente aceptado; los más reputados bacteriólogos del mundo entero, pudieron comprobar que en todas las lesiones verdaderamente tuberculosas, se encontraba el bacilo de Koch a exclusión de cualquier otro.

Los cultivos, las inoculaciones, la preparación de la tuberculina, los ensayos de vacunoterapia y sueroterapia, no hicieron más que afirmar con mayor fuerza si es posible, el descubrimiento de Roberto Koch.

En época muy reciente, algunos autores y entre ellos Jaime Ferrán, niegan la especificidad de este organismo microbiano, creyendo que la tuberculosis es un complexo clínico, que empieza por una labor química lenta y silenciosa, cuyo agente no es el bacilo de Koch.

El autor arriba mencionado dice:

La tuberculosis espontánea comienza casi siempre como una labor química lenta y silenciosa provocada por un tóxico bacilar que localiza su acción en los eritrocitos partiendo de la red linfática. Los glóbulos rojos se modifican de modo que se muestran más sensibles y sucumben más o menos fácilmente a la acción destructora de los eritrófagos viscerales.

En otra parte continúa:

En cuanto al agente de estas inflamaciones cuando son espontáneas, en vez de ser el bacilo de Koch, ácido resistente, lo es un ancestral suyo no ácido resistente, dotado en su origen de aptitudes saprofíticas y por lo tanto muy fácil de cultivar.

El Profesor Luis Renon, en su magnífica obra sobre las enfermedades populares, participa de las ideas de Ferrán y hace notar que ya el 20 de abril de 1886 Duguet y Héricourt, en una comunicación a la Academia de Medicina, dudaban del carácter específico del bacilo de la tuberculosis y se preguntaban si no era este microbio otra cosa que una de las fases evolutivas del Microsporon furfur. Las experiencias de estos sabios no merecieron llamar la atención y sólo muchos años después, es que Piory y Renoux, volvieron a buscar la comprobación de los primitivos estudios y consiguíeron mediante la inoculación de las escamas de la pitiriasis versicolor, producir en el cobayo una tuberculosis clásica.

Otros observadores, Ernest Lichtenstein, Georges Mayer, Paul Courmont, encuentran en la manteca y en lesiones aparentemente tuberculosas, bacilos que difieren del de Koch en algunos caracteres, pero que participan con este de la propiedad de ser ácidos resistentes. Finalmente el Dr. Santini en un interesante artículo publicado en la Revista de Higiene y Tuberculosis de Valencia, declara que habiendo hecho varias experiencias con el bacilo Ferrán; en uno de los casos la inyección repetida de bacterias atóxicas, determinó un proceso tuberculógeno, que ocasionó la muerte del animal, en cuya autopsia se encontraron tubérculos verdaderos.

Sin entrar a un estudio más profundo de las teorías del Profesor Ferrán y reduciéndolas a su mayor sencillez, podríamos condensarlas en las siguientes palabras: La tuberculosis no es una enfermedad producida por un solo bacilo, sino por toda una familia de bacilos saprófitos, que poco a poco y por distintas génesis, adquieren la propiedad ácido resistente.

Respetando las opiniones del célebre bacteriólogo español, al que tantos y tan importantes servicios debe la ciencia, debo declarar que la teoría saprofitaria de la tuberculosis, no se encuentra de acuerdo con las investigaciones de laboratorio y que en los muchos y muy variados estudios que he efectuado sobre esta entidad mórbida, siempre he podido comprobar la unidad completa del bacilo de la tuberculosis. Es evidente que en los cultivos ocurren ciertos fenómenos que conviene mencionarlos aunque sea ligeramente y a cuya interpretación, sea debido quizá, el que se sospeche de la completa unidad del bacilo de Koch. Courmont, Nicolle, Marmorek y muchos otros experimentadores, habían hecho notar que en los cultivos se encontraban dos especies de organismos bacterianos, los jóvenes y los de mayor edad. Ahora bien, si se toma un cultivo de 20 o 25 días y se le somete al método Ziehl Nelsen, se observa que mientras una parte de los bacilos, es ácido resistente, la otra se decolora en su totalidad por el ácido nítrico al tercio.

Este fenómeno que se puede observar en cualquier laboratorio, ha sido posiblemente el origen que ha hecho suponer que el bacilo de Koch no era específico. En este punto conviene hacer notar, que la propiedad ácido resistente no la adquiere el bacilo sino con la edad y constituye uno de los caracteres de su completo desarrollo; pero el que en las preparaciones existan algunos bacilos que se decoloren, no puede autorizar, en mi concepto, a negar la unidad de la especie, tanto más cuanto que es observación corriente que las bacterias según la edad de sus cultivos, adquieren nuevas propiedades o pierden las que tenían.

Mucho se ha insistido sobre las manifestaciones tuberculosas que se han logrado provocar en el cobayo mediante la inyección de bacilos saprofitarios. Sin negar el hecho, cabría preguntar si en estos casos las inyecciones repetidas de cultivos bacterianos, no han desempeñado el papel de causa ocasional, despertando un proceso baciloso latente. No tendría nada de extraordinario el hecho si se reflexiona la susceptibilidad del cobayo con respecto al bacilo de Koch.

Origen de la tuberculosis en el altiplano andino.—No obstante que no existen documentos fehacientes, en los cuales pueda fundar conclusiones de carácter inamovible, basado en las consideraciones que a continuación expongo, creo que antes de la conquista de la América Meridional por los españoles, la tuberculosis en esta parte del continente era o sumamente rara o totalmente desconocida.

Examinando las causas que originan la tuberculosis, tenemos que se encuentran ocupando lugar de preferencia la acción del aire confinado y húmedo, la alimentación deficiente, en una palabra la pobreza tal como la conocemos hoy en las grandes ciudades, pues bien, examinado lo que aun hoy día ocurre en la raza indígena, vemos que su tendencia es vivir en chozas separadas en las que rara vez existen más de cuatro o cinco personas, pues cuando el hijo o la hija llegan a la edad adulta, dejan la casa paterna para constituir lejos de ésta un nuevo hogar. En estas condiciones la aglomeración que juega un papel tan importante en la etiología de la enfermedad de que nos ocupamos, no ha podido existir en el altiplano, en cuyas inmensas llanuras, los caseríos de los primitivos habitantes, se esparcían quedando entre ellos grandes distancias.

Causas físicas.—El tórax llamado raquítico, aplastado por las partes laterales y muy manifiesto en la región del esternón, que simula la quilla de barco o al pecho de gallina, ha sido considerado por la mayor parte de los tratadistas como siendo el terreno abonado para el desarrollo de la tuberculosis; las personas así conformadas tienen respiración deficiente y basta una causa ocasional cualquiera, para que la enfermedad se produzca atacando de preferencia los vértices pulmonares.

La etiología del tórax raquítico, es múltiple y las causas que le provocan son distintas en cada caso particular, existiendo sin embargo, algunas de carácter general, entre los cuales encontramos la falta de un cubaje de aire respirable suficiente, la falta de ejercicio y la alimentación de mala calidad.

Cubaje de aire respirable.—Los higienistas de unánime acuerdo, declaran que cuanto mayor es la superficie que pueda disponer cada habitante, la salubridad es mejor. En Francia según los reglamentos militares, para cada soldado existe una superficie de 3 metros y 75 centímetros, en Inglaterra nueve, en Alemania cuatro y en París tomando el conjunto de la ciudad 46 metros. La cantidad de aire respirable por persona, nunca debería ser menor de 65 metros cúbicos dentro de las habitaciones. Teniendo en cuenta estos datos, nos bastará reflexionar que los primitivos habitantes del Altiplano Andino, tenían a su disposición la infinita soledad de la pampa, la cual si se hiciera el cálculo para determinar la densidad de la población, tendríamos que quizá habría un habitante por cada 4 o 5 kilómetros. Respecto al cubaje de aire respirable, debemos señalar el hecho de que por hábito el indio no permanece dentro de su choza sino para dormir, el resto queda en pleno aire, sea ocupado en las labores del campo o en los pequeños quehaceres domésticos, los que realiza en el patio de la casa, en pleno sol y al aire libre. Como consecuencia lógica de lo dicho, se deduce que el confinamiento tan temido por los higienistas, no ha podido ser la causa de la bacilosis en la raza del altiplano.

La alimentación insuficiente.—La mala nutrición ocasionada por una alimentación insuficiente, es también otra causa productora de la tuberculosis, otra disminuyendo las defensas orgánicas y facilitando en consecuencia la invasion de los elementos bacterianos.

Examinando la historia de la América, es fácil convencerse de que esta parte del continente gozaba de singular bienestar, la carne la tenían en abundancia de la llama y la alpaca, además la papa, la oca y otros vegetales alimenticios, proveían ampliamente a las necesidades de los primeros habitantes. Finalmente siendo el aimara, lo mismo que el quechúa, no una raza nómada sino sedentaria y agricultora, no se concibe que existiendo cuantos terrenos laborables se podían desear, hubiera individuos que sufrieran por la miseria.

La luz cuya acción útil como tónico del organismo ha sido estudiado por el Dr. José Verdes, Montenegro, es indudable que obra en estas grandes alturas de una manera muy eficaz. Efectivamente es raro que en la altiplanicie andino, existan dos días sin que se vea la luz del sol, lo ordinario es que el astro rey permanentemente extienda sus rayos sobre la inmensa meseta andina y que sólo momentáneamente desaparezca para volver a presentarse pasada la tormenta, que de ordinario es de corta duración. Según Schrroter, la luz solar aumenta los cambios gaseosos y

naturalmente la actividad orgánica. Morin le atribuye una real influencia sobre el estado psíquico, lo que sosteniendo la moral del individuo, lo hace más resistente a las causas patológicas.

Hace muchos años que los fisiologistas han sentado el principio de que la función hace al órgano, en esta virtud el indio obligado a respirar un número mayor y más amplio de veces para evitar la acción perniciosa de la rarefacción del aire, es indudable que ha desarrollado sus pulmones robusteciéndolos en tal forma, que es muy difícil que fueran la presa fácil de la invasión bacilar.

El desarrollo considerable del aparato respiratorio en el indio, se puede hoy mismo comprobar con la mayor facilidad y bastará citar lo que ocurre con los indígenas que se presentan a los cuarteles para cumplir con el servicio militar obligatorio y que son sometidos al examen médico.

Según la mayor parte de los cirujanos militares, entre ellos Allaire, Robert Hamnond, Stolaroff, la aptitud para el servicio se puede deducir no solamente por la talla, sino también por el estado de desarrollo pulmonar, de manera que un buen soldado debe tener según Seeland, como perímetro torácico la mitad de la talla del individuo más 2 o 3 centímetros.

No obstante que estas medidas han perdido hoy algo de su importancia primitiva, es un hecho que merece llamar la atención el que en la generalidad de los reclutas indígenas, el perímetro torácico es mayor con seis y siete centímetros de la talla media del individuo.

Esta amplitud de la caja torácica, es sin género de duda, la que permite al soldado boliviano en alturas que varían de 3,000 a 4,000 metros sobre el nivel del mar, hacer marchas de 10 y 12 leguas por día, sin fatiga y conservando toda la aptitud para continuar el viaje al siguiente día. Teniendo la legua 4,225 metros, resulta que un cuerpo de ejército en 12 horas y frecuentemente en menos tiempo, puede hacer más de 50 kilómetros llevando todo su equipo, sin fatiga para la tropa y sin que se vean soldados rezagados por el cansancio.

Debo advertir que no es un hecho extraordinario el que menciono, sino lo que ocurre habitualmente y en la Historia Nacional, sobre todo durante el Gobierno del General Melgarejo, no son raros los ejemplos de marchas forzadas del ejército que en un día ha hecho hasta 100 kilómetros, entrando inmediatamente después de esfuerzo tan gigantesco en línea de batalla.

Riqueza globular.—Las investigaciones de Metchnikoff, Ehrlich, Bordet, Witte y Nicoll, han demostrado el papel que juegan los elementos globulares de la sangre en la defensa del organismo contra las enfermedades infecciosas. Estudios llevados a cabo en el Instituto Nacional de Bacteriología, nos han dado las siguientes numeraciones:

	Milímetro cúbico.		Milímetro cúbico.
O. N.	6,083,470	C. O	6,826,676
E. R.	6,553,863	N. Q	5,435,505
D. F.	7,146,666	D. Ll	6,925.340

Por el cuadro que antecede se ve que el término medio de glóbulos rojos por milímetro cúbico en La Paz, es de 6,498,585 y como al nivel del mar este número es sólo de 5,000,000 por milímetro cúbico, resulta que a 3,629 y a 4.000 metros de altura en que se encuentran las ciudades de La Paz y Oruro, hay un aumento de riqueza globular de 1,498,585 por milímetro cúbico sobre la proporción que existe al nivel del mar.

Papel del contagio.—Cha eau, Puech, Gerlach, Gunther afirman la facilidad con al cual la tuberculosis humana puede trasmitirse a la especie bo ina y como es justo, el hecho recíproco tiene que ser e idente o lo que es igual, que la tuberculosis bo ina, puede trasmitirse a la especie humana.

Hoy la trasmisibilidad de la tuberculosis animal al hombre, se encuentra perfectamente establecida y ha motivado las múltiples medidas higiénicas que los Consejos de Salubridad de todos los países han dictado para e itar la venta de la carne proveniente de animales enfermos.

No obstante las afirmaciones de Koch que ante el Congreso Internacional de la Tuberculosis reunido en Londres el 22 de julio de 1901 sostuvo que la tuberculosis humana y la bovina eran absolutamente distintas y que no era posible la trasmisión de la enfermedad de una especie a la otra, los trabajos del profesor Nocard, prueban hasta la evidencia que el contagio es real, siendo bastante para demostrar este hecho la muerte de los veterinarios Moses, Weimar, Walley, Jeusen que inoculados accidentalmente al hacer la autopsia de los animales enfermos, murieron a consecuencia de la tuberculosis.

Es indudable que probada la unidad perfecta del bacilo de la tuberculosis, se comprenda fácilmente la importancia del contagio producido en la especie humana por los productos de origen bovino. Algo más, el profesor Behring, ante el Congreso celebrado en Cassel en 1903, señala como la causa etiológica más frecuente de las lesiones bacilares del pulmón, a la infección del intestino contraída durante la época de la primera infancia por la leche infectada.

Hecho igual señala el Profesor Magburgo y los autores Gothan, Coppes y Priester afirman haber observado casos de tuberculosis intestinal, provocada por la ingestión de leche proveniente de animales enfermos.

No me extenderé más en estas consideraciones cuyo objeto no es otro que probar que no habiendo existido en la América ganado bovino antes de la conquista, es necesario también eliminar esta causa, cuya importancia hemos puesto suficientemente en claro.

Respecto a los medios que han obrado directamente sobre el bacilo impidiendo su desarrollo o atenuando su virulencia, mencionaré en primera línea la acción de la luz, que en mi concepto desempeña un papel preponderante.

Las experiencias de Candler, Migneco, Ramnonne prueban que la luz obrando sobre los esputos desecados o sobre los cultivos vivos, atenúa la virulencia de éstos, hasta el punto de que cincuenta o sesenta días después de una exposición a los rayos solares, el bacilo deja de ser patógeno.

La influencia de la luz sobre el bacilo tuberculoso tanto humano como aviario, he podido estudiarla especialmente, valiéndome de cultivos provenientes de los laboratorios de Francia y Norte América.

El resultado de mis observaciones es el siguiente: Cultivos en patata de bacilo aviario expuestos durante 10 días a la acción difusa de la luz solar en el Laboratorio, han dejado de desarrollarse resembrados en nuevos medios.

Cultivos en patatas de bacilo humano, dejados 15 días en las mismas condiciones, no se han desarrollado ni en patata, ni en caldo glucosado, ni en gelosa glicerinada.

Independientemente de la acción de la luz cuya importancia no me parece discutible, es evidente que en la atenuación de este bacilo, han entrado otros elementos aun no bien puestos en claro, pero cuya existencia es innegable. No creo que la disminución de presión atmosférica, haya obrado en este sentido, pues las experiencias llevadas a cabo en este respecto por D'Arzonval y Charrin han demostrado en forma clara y palpable, que el aumento como la disminución de la presión atmosférica, tienen escasa influencia sobre el desarrollo de las especies bacterianas. Es más posible que la raza americana, en especial la del altiplano, haya ofrecido en el primer momento y por las razones ya apuntadas, una resistencia organica más grande. El hecho de observación es que el bacilo de la peste bubónica, el bacilo de Koch y quizá otros más, en el continente americano, son menos temibles sobre todo en determinados puntos, que lo que son en Europa o Asia. Así el bacilo de Yersin, a pesar de existir en forma endémica en casi toda la costa del Pacífico, nunca ha provocado las terribles epidemias que siembran el pánico en la India, Rusia y otros países.

Las distintas consideraciones mencionadas en los capítulos que anteceden, creo que me autorizan a sentar la teoria de que la tuberculosis humana no ha existido en la altiplanicie andina, hasta la época de la conquista española.

Junto con la civilización vinieron a la América, varias enfermedades, que consigo trajeron los españoles, pero la acción del clima, la natural defensa globular de la raza, hicieron que estas entidades mórbidas se propagaran muy poco.

Es necesario en mi concepto, llegar a una época relativamente reciente, para encontrar el origen real de la tuberculosis en la altiplanicie así como las causas que motivaron su difusión.

Las ciudades construidas por los conquistadores, que poco a poco fueron aumentando en actividad y población, eran como la mayor parte de las fundaciones españolas, insalubres bajo todos respectos, faltas de alcantarillas, con calles estrechas, algunas de las cuales como la Calle Linares, el callejón de Tiquina, la calle del Inca, la calle Muñecas, la calle Catacora y muchísimas otras que aun en la actualidad existen, apenas si miden de uno a tres metros de ancho. Añádase a esto que las casas del Coloniaje, eran estrechas, de techo bajo, puertas esencialmente pequeñas y faltas de aire y de luz. De estas casas, quedan aun muchísimas y al respirar el aire húmedo y frío de sus habitaciones, uno piensa en los sótanos de las grandes ciudades o en las malsanas prisiones que tanto prodigaron los tiranuelos de la Edad Media. Al contemplar esas casas donde sólo de tiempo en tiempo asoma temeroso un rayo de luz, es casi imposible explicarse satisfactoriamente, el por que de tan extrañas construcciones. Lo más racional es suponer que para resguardarse del frío y de los vientos helados de la cordillera, en un país donde el combustible es caro y difícil de conseguir, los primitivos pobladores quisieron defenderse de las bajas temperaturas reduciendo hasta lo inverosímil el tamaño de las puertas y ventanas y bajando el techo hasta el punto de que se lo podía tocar con la mano. Seguramente pensaron los primitivos pobladores, que impedir la libre entrada del aire, era disminuir los rigores del invierno y conservar el calor que da flexibilidad a los músculos y alegría al corazón; Pero a que precio se pagaba ese poco de calor!

Los indios habían sido obligados por los terratenientes a hacer el servicio en las ciudades y ya sea mensual o semanalmente venía uno de ellos con el nombre de pongo a La Paz u Oruro a servir a los patrones. Encerrado el indio en un medio que tan poca armonía guardaba con su vida libre y activa, es seguro que empezó a sufrir las consecuencias de esta reclusión y como numerosos enfermos venían ya en esas épocas a curarse de sus afecciones pulmonares, es pues fácil suponer que el quichua y el aimara alejados de su medio habitual, ofrecieron un terreno fácilmente vulnerable. Si se tienen en cuenta las pésimas condiciones higiénicas de la mayor parte de las ciudades bolivianas, es digno de llamar la atención el que la tuberculosis no hubiera extendido sus estragos en mayor proporción y que relativamente la mortalidad por esta entidad mórbida sea poco elevada.

La mortalidad por tuberculosis en los distintos estados, sería según el profesor Calmette de Lille, la que se menciona en el siguiente cuadro tomado del No. 83 de la Revista de Higiene y Tuberculosis del Dr. J. Chabás:

Estados.	Población.	Mortalidad total por 10,000 habitantes.	Mortalidad por tuberculosis por 10,000 habitantes.	Mortalidad por tuberculosis por 100,000 habitantes.	Mortalidad por tuberculosis por 100 óvitos de toda clase.
Alemania	62,849,563	186.6	17.8	15.4	10.1
Inglaterra	35,348,780	147.2	15.9	11.2	10.8
Austria	27,900,924	225.0	30.4	.....	13.5
Bélgica	7,386,444	165.1	13.0	10.1	8.3
Dinamarca	2,635,000	154.4	17.6	13.3	11.7
Escocia	4,826,587	161.3	19.6	12.6	12.2
España	19,712,585	260.2	18.5	13.6	7.4
Francia	39,196,328	190.0	22.6	18.7	12.3
Grecia	2,631,952	238.3	33.9	24.8	14.4
Hungría	20,786,278	244.4	37.0	.....	15.1
Irlanda	4,371,455	175.9	25.8	19.5	14.8
Italia	34,129,304	225.6	16.6	10.5	7.4
Noruega	2,321,575	142.9	24.4	18.8	19.3
Países Bajos	5,784,232	150.2	16.2	12.0	11.7
Portugal	5,432,132	226.4	11.8	9.9	7.8
Rumania	6,771,722	258.7	30.9	25.1	11.9
Suecia	5,377,713	141.1	26.7	20.7	19.0
Suiza	3,554,672	162.3	24.1	17.3	15.5

Los fallecimientos por tuberculosis en la mayor parte de las grandes capitales, tomando la proporción por cada 10,000 habitantes es la siguiente según el señor Abel J. Olachea:

Londres	14.43	Hamburgo	20.56
Buenos Aires	18.66	Breslau	38.27
New York	21.56	Madrid	26.33
Berlin	24.70	Leipzig	23.51
Paris	38.02	Munich	28.71
Viena	33.32	Roma	17.63
Filadelfia	19.73	Venecia	19.77
Dresde	23.36	Bruselas	17.29
Cologne	69.60	Stokolmo	23.42
Budapest	38.30	Praga	33.40
Copenhague	21.26		

En La Paz según los datos suministrados por el Boletín de Higiene y Demografía, el número de fallecidos por lesiones tuberculosas de los distintos órganos ha sido en 1913 de 134. Suponiendo ahora una población total de 100,000 habitantes, no tendríamos sinó 13.4 por 10,000, cifra seguramente la más baja de todas las que registran las estadísticas, pues aun comparándola con la de otras ciudades americanas, como por ejemplo Lima, cuya mortalidad en 1906 fué de 72 por 10,000, tendríamos que es un hecho indudable que las lesiones bacilosas aunque aclimatadas en La Paz, no producen los destrozos que en otras capitales.

Otra de las causas que ha motivado el aumento de la tuberculosis en el altiplano, es la inmigración de individuos enfermos, que han venido de la costa del Pacífico aprovechando de la favorable influencia del clima, a curarse, y como con ellos no se ha tomado ninguna precaución, que sirva de garantía, han ido esparciendo los gérmenes del mal hasta tal punto, que a continuar las cosas como hasta hoy, no será raro que se tenga que lamentar la más funesta influencia en nuestras estadísticas sanitarias.

La tuberculosis actualmente en La Paz como en Oruro, ataca de preferencia a los adultos, en los cuales tiene tendencia marcada a localizarse en el aparato respiratorio. Según el Boletín arriba citado, tenemos en el cuadro de defunciones la siguiente clasificación durante el año 1903.

Tuberculosis pulmonar	97
Tuberculosis laríngea	18
Tuberculosis intestinal	7
Tuberculosis generalizada	10
Mal de Pott	1
Enteritis tuberculosa	1
Total	134

Examinando el cuadro que antecede, vemos la inmensa preponderancia de la tuberculosis del aparato respiratorio sobre la de los demás órganos.

La causa de este fenómeno, sería en mi concepto la siguiente: La mayor parte del elemento joven de Bolivia, muy especialmente en las regiones mineras de Potosí, Oruro y La Paz, se dedica a la explotación de las minas de plata, cobre, estaño, wolfran y otros metales. En las grandes profundidades a que llegan los obreros, las minas se hallan desprovistas, en su inmensa mayoría, de todo principio de higiene y van respirando una atmósfera permanentemente cargada de partículas metálicas, que depositándose en los alveolos pulmonares provocan estados bronquiales agudos, que repitiéndose con frecuencia, finalizan en dilataciones bronquiales más o menos extensas, que son el terreno abonado de la tuberculosis.

En el elemento infantil, las lesiones bacilosas son sumamente raras y durante el año que me encuentro a cargo del Consultorio Público de Niños y del Pabellón respec-

tivo en el Hospital Landaeta, no he tenido ocasión de ver sino poquísimos casos de lesiones tuberculosas, que se las podrían clasificar en el siguiente cuadro: Calculando el número de niños asistidos durante el año de 1914 en 1,759 tendríamos que sobre este total las lesiones tuberculosas se encuentran representadas como sigue:

Tuberculoma del cerebelo	1
Artritis tuberculosa	1
Pleuresía purulenta de origen bacilar	2
Mal de Pott	1
Enteritis tuberculosa	1
Total	6

En mi práctica particular, he visto de igual manera muy pocos niños con lesiones bacilosas y entre éstos, la mayoría si no la totalidad, corresponden a los que habían permanecido en la costa o venían con el objeto de curarse.

Sabemos bien que existe una ley debida a Peter que ha dominado la patología de la tuberculosis y es la que dice que el niño nace tuberculizable no tuberculoso; en esta virtud la excesiva rareza de esta enfermedad en la infancia, conduce a pensar que los progenitores se encuentran indemnes, pues hoy se conoce el mecanismo del contagio que consiste, en que estando enfermos los padres a cada momento van sembrando el aire que respira el niño con millones de organismos patógenos, los que solamente esperan una causa ocasional, para desarrollarse en el organismo infantil.

Las últimas investigaciones respecto a la tuberculosis, tienden a quitar a la fórmula de Peter, su carácter absoluto y consideran junto a los niños tuberculizables, los que nacen enfermos y han recibido por intermedio de la sangre materna el germen del contagio.

El Profesor Landouzy, impresionado por la frecuencia con la cual a la autopsia de niños menores de dos años se encontraban lesiones tuberculosas, pensó que era racional suponer que la herencia o mejor la infección por intermedio del organismo materno, no era indiferente a esta multiplicidad de manifestaciones bacilosas. Para explicar el contagio del feto, los autores suponen que los cuerpos bacterianos, pasan por la vena umbilical para localizarse en el hígado o bien franqueando el conducto de Aransi se diseminan por toda la economía, dando origen a las formas generalizadas, cual han tenido ocasión de observarlas Facoli, Lehmann, Houl.

La trasmisión intraplacentaria es pues evidente, pero conviene hacer notar que es a todas luces rara y que en la etiología de la tuberculosis no juega sino un papel secundario.

A las numerosas pruebas acumuladas en capítulos anteriores, aun podríamos añadir otra, cuya significación es no menos importante. Todos los médicos que ejercen en La Paz, Potosí u Oruro, saben que los indios que no han salido de sus tierras, llámenseles comunidad, hacienda o sayaña, nunca presentan lesiones tuberculosas, siendo al contrario notable su robustez, su resistencia a los más duros trabajos y su increíble sobriedad. El indígena para trabajar doce horas, casi sin tomar descanso, no necesita otro alimento que un poco de charque o chalona (carne desecada de vaca y cordero respectivamente) un poco de maíz cocido o tostado y 200 o 300 gramos de hojas de coca, que mastica constantemente. Con una ración nutritiva de tan poco valor, el natural del país realiza los mayores esfuerzos, sin que su organismo sufra el menor quebranto.

Muy distinto es el porvenir del quechua y el aimara que se radican en las ciudades o que dedicados al pequeño comercio, viajan a los Yungas (regiones cálidas de la República, donde se producen el café, la coca, el cacao, etc.) o a la costa del Pacífico. En estos, pronto se presentan las pruebas inequívocas del mal y raras veces se logra detener su marcha invasora.

Respecto al estudio experimental del bacilo de Koch, poco tengo que añadir lo que dije en la Memoria presentada al Décimo quinto Congreso Internacional de Hi-

giene y Demografía reunido en Wáshington del 23 al 28 de septiembre de 1912, al que me tocó el honor de asistir como delegado oficial del Gobierno de Bolivia.

En dicho estudio, hice notar que en los cobayos, la inoculación de esputos en los que el examen microscópico había puesto de manifiesto numerosos bacilos, daba lugar a reacciones muy distintas de las que señalan como normales los autores que se han ocupado especialmente de este género de investigaciones.

Macé, Besson, Miquel, Cambier, Dopter y Sacquepée en sus obras clásicas, manifiestan que para el estudio de la virulencia, de los productos tuberculosos, el animal de elección es el cobayo, en el cual la inoculación subcutánea de productos bacilosos, determina fatalmente la tuberculosis y provoca la muerte en un plazo que varía de tres semanas a tres meses.

Inyectando bajo la piel un producto tuberculoso diluído en un poco de agua, hacia el décimo día se observa en el animal una pequeña induración, que se ulcera tomando el tipo tórpido y al mismo tiempo los ganglios inguinales se infartan.

A la autopsia, el hígado, el bazo, la superficie de los riñones, se encuentran cubiertos de múltiples granulaciones tuberculosas. Si se siembran los productos sospechosos en suero glicerinado, a la tercera semana se pueden ver las primeras colonias que bajo el aspecto de puntos blanco grisáceos, de superficies desecadas, empiezan a desarrollarse.

Al lado de esta descripción clásica, debo hacer notar las particularidades que la inoculación de productos tuberculosos ofrece en estas alturas.

Desde luego la muerte de un cobayo inoculado por la vía subcutánea, solo he podido observar una o dos veces sobre más de 200 animales en experiencia, lo ordinario es que después de ligera reacción local con infarto, el cobayo recobre su peso primitivo y en ocasiones hasta aumente, como ocurre en las observaciones 3, 7 y 9. Cuando el animal es sacrificado a la cuarta o quinta semana, se encuentran numerosos folículos en la superficie del hígado, en el bazo y en los riñones, pero estos productos sembrados en suero glicerinado, no obstante todas las precauciones que se tomaren, es muy raro que den origen a un cultivo positivo.

La interpretación de este fenómeno sería en mi criterio la siguiente: El bacilo ya por sí más frágil, menos virulento que el de otros países, no habiendo podido producir la muerte del cobayo, pierde por completo sus propiedades vitales, de suerte que el cultivo es nulo.

El siguiente cuadro que abarca las observaciones efectuadas del 7 de enero al 13 de junio de 1914, es particularmente importante y su examen confirma la opinión que sostengo.

Observación de cobayos tuberculosos.

Número y color de la cobaya.	Fecha de la inoculación.	Naturaleza del producto.	Peso primitivo.	Peso a la fecha.	Lesiones observadas.	Temperatura.
			Gramos.	*Gramos.*		*8 hs. 3 p. m.*
1. Cobaya café.....	Enero 7 de 1914.	Esputo tuberculoso.	635	590	Infartos ganglionares.	39°
2. Cobaya amarillo obscuro.	....."	....."	510	332	Infartos diminutos	38° 8
3. Cobaya amarillo claro...	Enero 8 de 1914.	....."	520	675	Úlcera en el punto inoculado.	38° 8
4. Cobaya amarillo obscuro	....."	....."	620	515	Úlcera con edema en el testículo.	39°
5. Cobaya café con blanco.	Enero 23 de 1914.	....."	415	351	Un débil infarto ganglionar.	38° 8
6. Cobaya blanco con amarillo.	....."	....."	540	553	Infartos ganglionares.	38° 8
7. Cobaya amarillo con blanco.	....."	....."	560	370	No posee ningún desarrollo.	39°
8. Cobaya blanco íntegro..	Abril 26 de 1914.	....."	625	632	Pequeña úlcera....	38° 7
9. Cobaya blanco cabeza negra.	Junio 13 de 1914.	....."	362	338	Una gran úlcera en toda la región abdominal.	38° 8

Alcoholismo y tuberculosis.—Duclaux, Renon, Bertillón sostienen la relación íntima que existe entre el alcoholismo y la tuberculosis y el segundo de estos autores dice textualmente "El alcoholismo crónico, ofrece el terreno abonado y fértil para el desarrollo del bacilo tuberculoso." Teniendo en cuenta la relación íntima del alcoholismo con la bacilosis, es indudable pues, que allí donde menos se consuma alcohol, será también donde la enfermedad haga menores estragos.

Sentado este principio y contra lo que algunos escritores muy a la ligera, sin observaciones completas y guiados por el examen superficial de los hechos, han sostenido, que la raza indígena es alcohólica en grado eminente, debo levantar la falsa imputación con que se infama gratuitamente a esta pobre raza, declarando con conocimiento pleno, que el indio muy lejos de ser alcohólico es esencialmente sobrio y cuando se embriaga, lo hace exepcionalmente y solo en las grandes fiestas, en las que olvida su miserable condición, para ahogar un momento en el licor, los sufrimientos que le abruman.

Investigando con criterio sereno lo que pasa en toda población indígena, cualquier escritor imparcial, no podrá menos de quedar admirado de la sobriedad del indio, que en un año, es excepcional que beba más de tres o cuatro días, dedicando el resto al trabajo.

A la embriaguez, por accidente y en tiempos demasiado alejados, no se le puede llamar alcoholismo, nombre con el cual, la ciencia designa a la costumbre, al hábito inveterado, de consumir bebidas fermentadas o destiladas.

Antes de la conquista, el indio no consumía otro licor que la chicha, que la obtiene haciendo fermentar el maíz y cuyo grado alcohólico es demasiado bajo para provocar lesiones viscerales graves y aun la chicha cual ya hemos dicho en otro punto, solo la tomaban en sus grandes regocijos.

La ausencia de hábitos alcohólicos, es indudable que constituye otra razón para suponer que la tuberculosis no se presentó en el Altiplano sino en época posterior y cuando mediante la venta de alcoholes de pésima calidad, la civilización empezó su labor educadora, por destruir esta raza, intoxicándola.

Profilaxia.—La profilaxia contra la tuberculosis debería ser la obra común de todos los gobiernos americanos, de suerte que se pueda emprender una acción en conjunto, cuyos resultados obren en bien de las nacientes sociedades del Nuevo Mundo.

El ejemplo de Alemania me parece digno de ser imitado, en ese pueblo cuyos estadistas son esencialmente prácticos, no se ha puesto el menor reparo para gastar sumas casi fantásticas, con tal de disminuir la mortalidad por la tuberculosis reduciendo sus estragos a la menor cifra posible.

En la América Latina no obstante de que tanto en las naciones que colindan con el Oceano Pacífico, como aquellas que se encuentran a orillas del Atlántico, la tuberculosis ha tomado un desarrollo alarmante, pocas son las repúblicas que hayan emprendido una lucha eficaz contra esta enfermedad social. En esta labor de civilización, tres son los pueblos que hasta hoy se han distinguido por su benéfica actividad: el Uruguay, la república de Cuba y la gran nación argentina. En Cuba y en la República Oriental, la campaña es enérgica y ha dado hasta hoy muy apreciable frutos, merced a la inteligencia y esfuerzo de notables científicos, entre los cuales sólo citaré los nombres de Juan Santos Fernández, Francisco J. de Velasco, Carlos M. Desvernine, Arturo G. de Tejada, y Oscar Jaime de la Habana y Tomas Hernández de Sagua La Grande. En el Uruguay los Drs. Sebastián B. Rodríguez, Arturo Garabelli y Ernesto Fernández Espiro.

En la República del Plata, el iniciador de la campaña contra la tuberculosis fué el Dr. Enrique Tornu, que en el año 1898 trazó un plan general de profilaxia antituberculosa.

Posteriormente el Dr. Samuel Gache, Roberto Wernicke y otros más, se propusieron fundar la Liga contra la Tuberculosis. Finalmente el Dr. Emilio R. Coni, fué el que en la Argentina ha fundado prácticamente la lucha contra la tuberculosis, creando

en mayo de 1901 la Revista "Alianza de Higiene Social", que tantos beneficios ha prestado a la ciencia, haciendo que su director merezca la gratitud nacional.

A título de conclusiones y para no extender más el presente trabajo, voy a proponer al Segundo Congreso Científico Panamericano que si cree conveniente adopte las siguientes resoluciones, algunas de las cuales formaron parte del Primer Congreso Latinoamericano reunido en 1901.

1°. Los Gobiernos de Norte, Centro y Sud América, mediante sus delegados se comprometen a organizar con carácter de servicio público, la lucha contra la tuberculosis.

2°. Para los efectos del artículo precedente, se organizará en Wáshington u otra ciudad que designare el Congreso, un comité central que fijará las bases de la lucha antituberculosa.

3°. Los distintos Gobiernos contribuirán mediante sumas proporcionales, al sostenimiento de este comité.

4°. Cada dos años se reunirá una asamblea de delegados en la ciudad en que funcionare el comité central. A esta asamblea concurrirá cada Gobierno mediante sus delegados, para poner de manifiesto las medidas que se hubieran adoptado en cada país, para la lucha contra la tuberculosis.

5°. El comité central haciendo uso de los medios que se encuentren a su disposición, procurará que en cada República se organicen ligas contra la tuberculosis.

6°. Para mejorar las condiciones higiénicas del obrero, el comité dictará los reglamentos respectivos, que serán sometidos a la aprobación de los distintos Gobiernos.

7°. Para facilitar la curación de los enfermos, el comité central hará que se estudien los puntos más apropiados en los cuales se pueda fundar sanatorios especiales, para cuya construcción los distintos Gobiernos contribuirán con sumas distribuidas prudencialmente según los recursos de que puedan disponer.

8°. La declaración de las tuberculosis abiertas, será obligatoria para el médico.

9°. El consumo de la leche debe ser comprobado por veterinarios oficiales, que investiguen la sanidad de las vacas lecheras.

10°. Se recomiendan los ejercicios de la cultura física, como un medio de lucha contra la tuberculosis.

11°. Se declara obligatorio en los establecimientos de instrucción primaria, el uso de una cartilla que contenga los fundamentos de la profilaxia antituberculosa.

PROFILAXIA DE LA TUBERCULOSIS.

Por CONSTANCIO CASTELLS,

Médico del Hospital "Fermín Ferreira," de Uruguay.

"La salud del pueblo, la salud de los hombres, es la suprema ley."

Teniendo trascendental importancia el poner en práctica el mayor número posible de medidas profilácticas tendientes a prevenir y evitar el progresivo desarrollo de la tuberculosis, bosquejaremos en breves párrafos y sin profundizar en la materia debido a la índole sintética de este trabajo, los principales puntos que abarca dicho problema.

Dichas medidas las clasificamos en tres grupos: Del primero forman parte todas las que se consagran a suprimir el contagio directo es decir el que pueden provocar los enfermos bacilares, entrando en el mismo, las medidas higiénicas y por medio de antisépticos y desinfectantes, recomendados para destruir los bacilos tuberculógenos, los focos purulentos, esputos, etc., neutralización de toxinas, etc., corrientemente puestos en práctica.

El contagio volátil según la teoría de las gotitas micróbicas, los llamados gases alimentos de bacilos, las neblinas de microbios, sólo visibles al ultramicroscopio y que se acumulan en las inmediaciones de un contagioso constituyendo zonas peli-

prosas; son también tributarias del uso de diversos desinfectantes para su destrucción. Se han preconizado para ello el uso del aerofiltro, las fumigaciones, termovaporizaciones, etc., a base de distintas drogas, procedimientos todos muy recomendables y que tienen por base la difusión de sustancias antisépticas a la par que balsámicas para las vías respiratorias del enfermo.

Se recurrirá a las fumigaciones cuando no se pueda practicar el aislamiento del enfermo y tengan que atenderlo de cerca otras personas sobre todo durante la noche, proporcionando así un aire purificado aunque artificialmente evitando o disminuyendo los peligros de la auto-infección y contagio.

La desinfección corporal del enfermo, ropas, muebles, útiles, escupideras, etc., las recordamos por tener suma importancia su escrupulosa práctica, así como la destrucción de los portadores de gérmenes, insectos, etc.

En el segundo grupo hemos reunido todos los medios de que disponemos para reforzar la inmunidad del organismo en los sanos y enfermos.

El conocimiento etiológico de la tuberculosis, y su evolución permiten fijar los medios profilácticos reforzadores de la inmunidad estableciéndolos sobre sólidas bases: el tubérculo es considerado como un residuo morboso y la enfermedad tuberculosis representada orgánicamente como una discrasia, resultante de las alteraciones del metabolismo bioquímico provocado por la acción toxi-infecciosa de las bacterias no-ácido-resistentes (períodos pretuberculosos) las cuales son ancetras del bacilo de Koch. Es pues en este período que debemos reforzar la inmunidad para evitar la formación de tubérculos.

Los trabajos clásicos de inmunoterapia han demostrado que las bacterias aisladas del período crónico de esta enfermedad carecen de vacuna.

La profilaxia ideal pues estaría representada por la inmunización del organismo contra las bacterias del período agudo o tuberculógenas pero en los trabajos tendientes a su obtención están preocupados eminentes bacteriólogos, Ferrán de Barcelona entre ellos y no es posible todavía formar criterio exacto sobre su positivo valor, pero esperamos que un feliz éxito corone sus experiencias y no se malogren las esperanzas que en ellos tenemos depositadas.

Triste para nuestro siglo tenerse que esclavizar a un bacilo. Nada en verdad reuniría mayor número de ventajas para hacer buena profilaxia antituberculosa, que conseguir una vacuna específica.

La discrasia fímica tiene el gran inconvenientae de ser de muy difícil diagnóstico en sus comienzos y se confunde generalmente con otros sindromos. Con los recursos ordinarios de la exploración clínica se diagnostican las formas vulgares de tuberculosis pulmonar pero son infinidad los organismos que reaccionan positivamente a la tuberculina (tubérculo reacción) a pesar de no sospecharse clínicamente la existencia de tubérculos.

El organismo posee alguna inmunidad (anticuerpos de los extremos globulares) pero la pierde fácilmente según variadas circunstancias, entre las más aceptadas cítanse la predisposición humoral del terreno por inpregnación específica y tóxica, la llamada aptitud bio-química, desmineralización y descalcificación. La acción bioquímica de las sales de calcio evitando la desmineralización y descalcificación reforzaría también las defensas orgánicas en contra de la infección tuberculógena.

Entre las circunstancias ocasionales de la pérdida de inmunidad tenemos el contagio directo de que antes hamos hablado y el indirecto entrando entre éstas, la edad, lactancia, pubertad, vida genital, desgastes, enfermedades intercurrentes, etc.

Mientras no sea pues un hecho la aplicación de una vacuna específica o una sustancia bioquímica (Quimioterapia) que consiga la inmunidad antituberculosa, la profilaxia toma todo el carácter de social o colectiva y es en este, tercero y último grupo que pasaremos revista a los interesantes puntos que abarca. Indudablemente hoy por hoy el problema de la profilaxia antituberculosa es sobre todo social.

Se ha llegado a la afirmación (Grancher) de que la tuberculosis es de las enfermedades crónicas la más curable, dependiendo únicamente de la resistencia individual

y de los cuidados higio-dietéticos, pues bien con más seguridad afirmamos nosotros que es la más evitable poniendo en juego todos los resortes de cultura profiláctica, fomentando la instrucción práctica y haciendo conocer el peligro tuberculoso que como dice Babinsky, "es universal y avanza lenta pero seguramente."

Consultando las estadísticas de distintos países vemos elocuentemente demostrado que la mortalidad por tuberculosis está en razón inversa del grado de cultura y de las medidas de profilaxia social que en ellos se toman.

No se hace profilaxia donde hay analfabetos, ¿resultan acaso útiles para ellos los carteles y avisos de "se prohibe escupir" "no se permite fumar," etc.? Se generalizan acaso entre ellos reglas de higiene? Todo lo contrario. Los analfabetos se trasmiten sus costumbres y ciertas prácticas que ellos quizás creen de utilidad pero que están reñidas con las más elementales reglas de higiene y que entrañan serios peligros.

Cuando se dan cuenta de que el flagelo ha hecho presa de ellos acuden a los dispensarios y hospitales, sociedades benéficas, etc., impetrando un socorro pero casi siempre llegan tarde y en tales condiciones dichos establecimientos de asistencia gratuita no pueden llenar las sentidas necesidades de los que a ellas acuden acosados por el terrible mal.

En el Uruguay funciona desde hace algunos años persiguiendo fines profilácticos, la Liga Uruguaya contra la Tuberculosis, meritoria institución muy bien organizada pero que debido a la enorme cantidad de las personas que acuden para beneficiarse de su bienhechora acción no le alcanzan los recursos disponibles.

¿La ley de seguros contra esta enfermedad remediaría este conflicto? Puede ser, útil la ley de seguros para obreros? Según Loc, dicha ley en Alemania donde hace algunos años se implantó empeoró la situacion del proletariado, pues se aumentaron los impuestos, creciendo a su vez las cargas para los pobres que son quienes en realidad las pagan, enfermándose por tener que trabajar en exceso y en malas condiciones en los talleres, fábricas, minas, etc.

Hemos dicho en malas condiciones de trabajo precisamente por que vemos por las estadísticas que éstas y no el trabajo excesivo es lo que influye en el aumento de la tuberculosis pulmonar.

La rápida ejeada que queremos dar a todas estas cuestiones no nos permite entrar en mayores detalles, haciendo resaltar que el ejercicio regulado y el trabajo reglamentado no provoca el desarrollo de la tuberculosis.

Opuestamente se presentan todos los días a nuestra observacion enfermos en cuyos antecedentes encontramos un exceso de trabajo y aun malas condiciones del mismo, por ejemplo madres de familia que estando en el período de lactancia tienen que trabajar en fábricas, talleres, etc.

Deben pues los gobiernos proteger el trabajo y reglamentar el de las mujeres y niños, ya que es difícil reformar la humanidad y más aún hacerla perfecta, se conseguirá más fácilmente mejorar las condiciones actuales y buscar por todos los medios su preservación y contagio.

La ciencia eugénica dedicada al estudio de las influencias capaces de perfeccionar el desarrollo de la raza humana para obtener el desiderátum de hombre sano se halla ligada íntimamente a la profilaxia tuberculosa.

Debe evitarse el engendro de seres enfermizos, que serán el día de mañana criminales, degenerados, que representan el baldón de la humanidad, convirtiéndose en carne de presidio u hospital.

La tuberculosis es el enemigo hereditario de la humanidad, una sangría continua, que siembra el llanto y la viudez, el desamparo y la horfandad de todos los países.

Se nos oprime el corazón al suponer que podemos quedar impasibles contemplando ese mal tan horrible y apocalíptico de la peste blanca, capaz de prevocar más víctimas que todas las guerras, catástrofes y calamidades reunidas.

Réstanos enumerar las cuestiones que encierran capital importancia como factor individual y social para la profilaxia tuberculosa.

Los peligros individuales podemos clasificarlos así:

La falta de higiene, corporal, doméstica, etc.

La predisposición hereditaria.

El retardo de desarrollo y crecimiento.

Falta de ejercicios al aire libre.

Falta de ejercicios de ginmasia respiratoria.

Habitación insalubre. Hacinamiento en la vivienda.

Contacto con otros enfermos, excesos, fatigas, falta de suficiente alimentación.

Tuberculización por alimentos sospechosos, leche mal hervida, adulterados.

El alcoholismo: educar sobre el inmenso peligro del alcohol.

Limitar el número de despacho de bebidas.

Favorecer en cambio el consumo de bebidas sin alcohol.

Castigar el fraude; aumentar las penas a los ebrios.

Estimular a los que no beben con premios o mejorando sus jornales.

Permitir solamente el consumo de alcohol puro y castigar severamente el fraude que se comete vendiendo alcohol de orujo, patata, trapos y hasta de tierras, que son tóxicos y se lucra hoy día con su fabricación.

Enseñar prácticamente estos peligroes a los analfabetos.

Para terminar este punto, favorecer por todos los medios la lucha contra el alcoholismo.

Combatir la miseria, fundando las cooperativas, asociaciones de socorros mutuos, cantinas escolares, restaurantes populares, etc.

Dictar leyes contra la usura.

Poner contribuciones a los vicios.

Proteger a la mujer embarazada, a la maternidad y a la tierna infancia.

Crear casas de salud destinadas especialmente a los organismos fácilmente tuberculizables o predispuestos como son escrofulosos, linfáticos, anémicos, etc.

Fomentación de las colonias escolares, escuelas al aire libre, estaciones campestres, siendo de gran utilidad las plazas de ejercicios físicos que actualmente funcionan ya en Montevideo con enorme éxito.

La profilaxis por lo que respecta a la higiene urbana es también de suma importancia, pues de aplicarse bien asegurarían, la vida normal y de gran resistencia a todos los trabajadores y empleados que no disponen más que de un reducido espacio para habitación con ventilación insuficiente, exponiéndolos a los graves peligros del hacinamiento, contagio, etc.

Inspección prolija de los mataderos, frigoríficos, de la leche, de los almacenes de comestibles, prohibir la venta ambulante en malas condiciones. Exigir el más estricto cumplimiento de las medidas de desinfección a las empresas de tranvías, carruajes, automóviles, ferrocarriles, etc.

Evitar el matrimonio entre tuberculosos y sobre todo tener en cuenta que de los dos progenitores es la madre la que de mayor predisposición, o herencia de terreno, y por lo que respecta al padre que no sea un alcohólico, sifilítico, canceroso, degenerado, etc.

Protección a la infancia ya que la tuberculosis del adulto se considera como un despertar de una infeccion o pérdida de inmunidad sufrida en los primeros años.

Recordaremos también la profilaxis de todos los insectos que se convierten en portadores de gérmenes.

Algunos otros puntos pudiéramos señalar pero nos contentamos con haber señalado los principales y cuya práctica es necesaria si realmente queremos que sea un hecho la profilaxia contra la tuberculosis.

Por lo expuesto se comprende que abarca un dilatado campo de acción, desde la moralidad de costumbres hasta el sacrificio material impuesto a las colectividades para aliviar a los pobres y desamparados, que se impone hacer verdadera educación

antituberculosa, por medio de folletos, conferencias, etc., y por todas las prácticas imaginables, comprensibles para las clases analfabetas.

En esa forma se hará sentir la infuencia social en tan importante problema interinamente se resuelve el trascendental de la inmunoterapia o de la quimioterapia, encontrando el específico ideal para inmunizar al organismo desde la más tierna infancia contra tan terrible mal.

Es necesario que las ciencias médicas, en este punto se hallen amparadas por los gobiernos y colectividades, porque únicamente está al alcance de sus investigadores el obtener prácticamente los trascendentales resultados de la inmunidad tuberculosa,

Hay que desechar de nuestra imaginación todo prejuicio y escepticismo al respecto, hay que esperanzarse de que su obtención en fecha más o menos lejana será un hecho, pero interinamente debemos todos con nuestro tributo social combatir esa plaga y buscar la salud favoreciendo y estimulando, cuanto la acrezca, y combatiendo y eliminando cuanto la oprima.

LA TUBERCULOSIS EN EL URUGUAY.

Por JOAQUÍN DE SALTERAIN.

Vicepresidente del Consejo General de Estadística del Uruguay.

La declaración obligatoria de las enfermedades infecto-contagiosas, existe en vigencia en el Uruguay desde las postrimerías del año 1896. La denuncia de los casos de tuberculosis pulmonar o laríngea, debe ser elevada ante las autoridades correspondientes, por los médicos, en las 24 horas después de comprobada la enfermedad, debiendo, asimismo, los referidos, aconsejar a las familias o personas que rodean al paciente, las medidas necesarias para evitar el contagio y propagación de la dolencia.

En la práctica, la medida en sí, no ha levantado protestas, ni producido serias dificultades, sino que por el contrario se ha incorporado a las costumbres, merced al ilustrado concurso del cuerpo médico y al convencimiento que en el espíritu del público se ha difundido por medio de la propaganda.

Gracias a esos factores, puede afirmarse que el aislamiento impuesto en la mayoría de los casos, a nadie repugna ni es mirado como un vejamen.

En este sentido, mucho le debe el país a la acción de las ligas contra la tuberculosis, cuyos pacientes desvelos llevados a cabo, con encomiable anhelo, de puerta en puerta, en las más humildes viviendas, han enseñado al obrero y al menesteroso, a precaverse y a precaver a los que los rodean, así como a confiar en las autoridades, encargadas de la salud pública. Con tan valioso concurso, la luz de la verdad ha penetrado en todos los hogares; los conocimientos relativos a los peligros del contagio se han vulgarizado en todas las esferas sociales, pudiendo asegurarse que no existe zona alguna en el país, aún en los parajes más apartados y desiertos, donde se ignoren.

La preparación inicial, indispensable, existe y con ello el terreno propicio para el desenvolvimiento de las disciplinas que han de conjurar numerosos desastres. Desde la promulgación de la ordenanza, haciendo obligatoria la denuncia de las enfermedades infecto-contagiosas, han sido declarados en el Departamento de Montevideo, como tuberculosos, los siguientes casos:

1897	71	1906	916
1898	484	1907	883
1899	742	1908	767
1900	802	1909	755
1901	740	1910	845
1902	832	1911	1,166
1903	1,153	1912	1,374
1904	1,012	1913	1,724
1905	989	1914	1,266

La profilaxis general de la tuberculosis humana y animal está regulada, excepción hecha de la acción ejercida por la asistencia a los hospitales y por las ligas contra la tuberculosis, por los siguientes resortes:

1. TUBERCULOSIS HUMANA.

Declaración obligatoria de la tuberculosis pulmonar y laríngea (1896);

Preceptos generales para evitar la propagación de la tuberculosis por los enfermos que padecen de la forma pulmonar y laríngea (1898);

Protección escolar contra la tuberculosis (1906);

Desinfección por los locales habitados por los tuberculosos (1903);

Prostitutas tuberculosas, curación y aislamiento (1906);

Preparación, venta y aplicación de la tuberculina (1911);

Desinfección obligatoria de los muebles y enseres usados, que se venden particular o públicamente (1893);

Profilaxis de la tuberculosis en el Ejército y la Policía (en proyecto), 1906;

Protección a los maestros de escuelas públicas, afectados de tuberculosis de las vías respiratorias. (en proyecto), 1909.

2. TUBERCULOSIS ANIMAL.

Vigilancia sanitaria de establos y lecherías.

Servicio de tuberculinización e inspección de veterinaria.

Intervención de la Dirección de Ganadería, en los casos de tuberculosis animal.

Ley de la policía sanitaria de los animales, que obliga el sacrificio de los animales enfermos y acuerda indemnizaciones a los propietarios.

ASISTENCIA AL TUBERCULOSO.

Además de esos medios, la asistencia pública atiende a los tuberculosos pobres, en los hospitales que dirige, en los Departamentos del interior y en la capital y de una manera especial en esta última, en pabellones aislados, construídos expresamente, en el denominado Hospital Fermín Ferreira. La última documentada memoria de la Asistencia Pública Nacional, y que alcanza hasta fines de 1912, decía a este respecto:

Hoy, el Hospital Fermín Ferreira tiene habilitados 13 pabellones para la asistencia de tuberculosos e infecto-contagiosos, con la siguiente distribución.

Pabellones de madera, Nos. 1, 2, 3 y 4 con 38, 40, 28, y 24 camas, respectivamente; tuberculosos mujeres.

Pabellón de madera No. 5 con 24 camas, dividido en cuatro secciones, para aislamiento de infecto-contagiosos, hombres y mujeres.

Nos. 6 y 7, pabellones de mampostería, gemelos, con 36 camas, respectivamente, divididos en seis secciones cada uno, para aislamiento de infecto-contagiosos hombres y mujeres. Por ser suficientes, en las condiciones normales, los otros pabellones de aislamiento, el No. 7 está casi siempre ocupado por tuberculosos hombres.

No. 8, Pabellón Docker con 24 camas destinado a leprosos.

Pabellones de mampostería, Nos. 9 y 10 con capacidad para 50 enfermos, cada uno, ocupados por tuberculosos hombres.

Pabellones Nos. 11 y 12, de madera, con 25 y 28 camas, respectivamente; tuberculosos mujeres.

No. 13, Pabellón Docker, 30 camas, ocupadas por niños.

El movimiento del referido hospital, en el año de 1912, fué el siguiente, por la tuberculosis: Existencia en 1 de enero, 320; ingresados, 1,178; total, 1,498. Fallecidos, 377; mortalidad, por ciento, 25.17. La proporción de 25.17 por ciento de mortalidad por tuberculosis en el Hospital Fermín Ferreira, no es, ni con mucho excesiva, pues la casi totalidad de los enfermos, acuden al establecimiento cuando el trabajo les es imposible. En la especie, se trata de casos graves en el último período de la enfermedad, cuando la formación de las cavernas, la fiebre hética y el aniquilamiento profundo del paciente, dejan pocas o ningunas esperanzas de mejoría.

En este sentido, la experiencia ha demostrado, que a pesar de la propaganda y enseñanza antituberculosas, difundidas, como hemos dicho, por los confines del país entero, y a pesar del conocimiento que el pueblo posee, acerca de las probabilidades de curación, en los primeros períodos de la tuberculosis; el enfermo se resiste a dejar su hogar y abandonar el trabajo, hasta que aquella agota sus energías. Por eso la población de nuestro hospital de tuberculosos está formada, casi exclusivamente, por individuos extenuados ya y por eso también los resultados obtenidos y que oscilan siempre alrededor de las proporciones transcritas, deben mirarse, relativamente, como muy favorables.

Pueden asimismo considerarse como elementos coadyuvantes, en favor de la profilaxis de la tuberculosis, los siguientes:

ASILOS MATERNALES.

La asistencia pública cuenta con cuatro establecimientos de esta índole.

Asilo maternal No. 1.—Situado en la parte sud de la ciudad nueva, bastante cerca de la costa marítima, ocupa una superficie de 930 metros cuadrados. Fué inaugurado en 1891.

Asilo maternal No. 2.—En la parte norte de la ciudad nueva. Ocupa una extensión de 958 metros cuadrados en 1890.

Asilo maternal No. 3.—En la vieja ciudad. Extensión 1,095 metros cuadrados, 1896.

Asilo maternal No. 4.—En los alrededores de la ciudad. Funciona conjuntamente con la Escuela del Hogar en una extensa manzana de terreno.

La población de los asilos maternales, en el año 1912 fué:

Asilos.	Días de clase.	Niños y niñas (asistencia total).
No. 1	231	89,047
No. 2	203	78,806
No. 3	204	68,891
No. 4	192	78,144
Promedio diario	.....	1.472

Estos establecimientos, por sus fines, y por su excelente organización, deben considerarse como factores positivos que cooperan en beneficio del niño, cuyos padres no pueden atender las necesidades del hogar, en razón de sus ocupaciones.

Una alimentación reparadora y sana, contribuye al desenvolvimiento orgánico regular y una enseñanza metódica, en relación con los perfeccionamientos de la moderna pedagogía, y que contempla las necesidades complejas de la infancia, vigoriza sus nacientes energías.

COLONIA DE VACACIONES.

Como los anteriores institutos de la capital, la colonia funciona, desde hace años, con positivas ventajas.

Está situada en la parte Sud de la ciudad, a orillas del mar, en un terreno de algo más de 15 hectáreas, donde abundan las plantaciones de pinos, eucaliptus y acacias, así como las de diversas hortalizas. Los asistentes a ella, nunca pueden ser enfermos, sino niños débiles, linfáticos y predispuestos.

Los resultados obtenidos, desde la época de su fundación, hasta la actualidad, han sido sumamente satisfactorios, pues según la autorizada opinión del ilustrado facultativo que la dirige, se ha comprobado siempre en los niños: el aumento de peso, el mayor incremento de la talla, como la amplitud del tórax: índices principales que se toman como elementos de comparación. El número de asistentes en los últimos años, ha sido: 1908 a 1911, 504; 1912, 81.

CONSULTORIO GOTA DE LECHE NO. 1.

Tiene por fines: Fomentar la lactancia materna, enseñar los primeros cuidados que las madres deben poner en práctica, vigilar y dirigir el crecimiento normal de los niños, prestar asistencia a los menores de dos años que concurran al consultorio y distribuir leche de la mejor calidad, entre los niños necesitados e hijos de madres menesterosas.

Está instalado en uno de los principales barrios obreros de la ciudad, poseyendo todos los aparatos necesarios para la esterilización de la leche, envases, etc.

En el año 1911 ingresaron 1,146 niños y en 1912 la cantidad llegó hasta 1,946.

Excepción hecha de los organismos a que hemos hecho referencia, pueden asimismo considerarse, como elementos destinados a preservar y amparar a los niños, el Asilo de Expósitos y Huérfanos, con su extenso servicio externo, numeroso personal de nodrizas y cuna, así como el Hospital de Niños y policlínica médica, quirúrgica y diversas especialidades.

También debemos mencionar el establecimiento de la nueva Maternidad, modelo en su género, que acaba de inaugurarse, en los momentos que escribimos.

ASISTENCIA Y CURA DEL TUBERCULOSO POR LA "LIGA URUGUAYA."

El 16 de junio de 1902, por iniciativa popular, se constituyó en Montevideo la "Liga Uruguaya," la cual desde su fundación emprendió una lucha activa y persistente para el triunfo de sus propósitos. A pesar de no estar preparado el ambiente, la tenacidad de sus iniciadores y la elocuencia de los hechos demostrados por una propaganda tan activa como eficaz, abrieron los ojos de las multitudes, que bien pronto comprendieron la importancia del problema que, por primera vez, se planteaba en el país con la serenidad que requiere.

La voz de alarma se propagó por los clubs, por las escuelas y por los cuarteles; la prensa, toda, acogió la iniciativa, apoyándola sin reticencias, y el público entero, de la ciudad y del interior contribuyó al éxito con loable interés, a punto tal que, meses después de constituirse, celebraba conferencias públicas, en Montevideo y en los departamentos, publicaba una revista y fundaba su primer dispensario de asistencia a los tuberculosos necesitados.

Para darse cuenta exacta del interés despertado por la intensidad de la propaganda, bastaría recordar que entre los centenares de donativos espontáneos que se repetían en todos los momentos, figuró el de un generoso anónimo con el terreno donde tiene su edificio modelo actualmente la institución. Y no satisfecho con eso, más tarde, donó también anónimamente, la cantidad de $100,000 oro uruguayo.

El Gobierno, a su vez, dándose perfecta cuenta de la importancia de la obra, la alentó con su vigorosa ayuda, subvencionándola más tarde con la cantidad de $24,000 anuales.

Gracias al concurso unánime del pueblo y de sus autoridades, inspirados ambos en nobilísimos propósitos, la liga ha podido desenvolver con eficacia su esfera de acción, obteniendo en varios de los concursos celebrados en el extranjero, las más altas recompensas. En la actualidad, prosigue, sin interrupción, la tarea emprendida, siendo de esperar que en el porvenir ha de ampliar y mejorar día por día, los servicios que de ella dependen.

En el mes de enero de 1914, al inaugurar la "Primera conferencia encargada de orientar la lucha contra la tuberculosis, en el interior del país," organizada por la Comisión Directiva de la Liga Uruguaya Contra la Tuberculosis, y que se celebró en Montevideo, del 18 al 23 del mismo, el ilustrado Presidente decía:

Nuestra liga gracias a los perseverantes esfuerzos de sus fundadores, y a los de su abnegado comité de damas, ocupa un puesto de primera fila entre las de la América Latina. En los 11 años trascurridos desde su fundación ha prestado asistencia a 3,774 enfermos, sometido a observación a 15,096 y dado de alta por curación o notable mejoría, aptos para el trabajo a 535. Ha distribuído 600,000 litros de leche, 400,000 kilogramos de carne, 270,000 kilogramos de pan, 14,300 pesos en subsidios de diversas

clases y gran cantidad de camas, colchones, ropas de abrigo y de vestir. En el solo año 1912–13 ha dado 33,162 baños y practicado gran número de desinfecciones a domicilio y en el desinfectorio.

Hoy, en sus tres dispensarios y en el sanatorio diurno, tiene bajo su protección y asistencia 592 enfermos y por la escuela al aire libre y la "Copa de leche," su acción preventiva alcanza a 650 niños. Como se ve, en la capital, la obra de la liga, es tan amplia como lo permiten sus recursos.

En los departamentos, la organización de las ligas, que había empezado a desarrollarse con la creación de dispensarios en Minas, Salto, Paysandú y Treinta y Tres, se detuvo de pronto y casi se paralizó en 1908 sobre todo por falta de recurso. sPocas comisiones departamentales daban señales de vida y fué necesario reorganizarlas en los últimos años con motivo de la colecta popular del Día de los Tuberculosos." El resultado de estas colectas y la decisión de la comisión central de dejar a cada departamento el producto respectivo, ha despertado nuevas energías y en la actualidad en todos los departamentos están constituidas las comisiones delegadas y los comités de damas.

COSTO DE LA ASISTENCIA AL TUBERCULOSO.

De una manera matemática, no es posible comparar exactamente lo que cuesta a la asistencia pública el tuberculoso, con lo que gasta la liga uruguaya, pues aunque a primera vista no parezca, se trata, en la especie de elementos heterogéneos. La administración, casi por lo general, atiende al enfermo en el último período de su dolencia, cuando postrado y débil, necesitando un exceso de alimentación, prolonga, a esa condición, su minada existencia, durante largos períodos de tiempo, si es que no se interrumpe pocos días después del siempre combatido ingreso al asilo, el epílogo de su agonía.

La tarea de la liga, es más amplia, pues que ensancha su esfera de acción tomando al sujeto, desde que se sospecha pueda estar enfermo, o hallarse en condiciones de susceptibilidad morbosa. Lo enseña a precaverse, lo ayuda y lo sigue dentro de la propia vivienda.

La asistencia acepta, porque no puede menos, los despojos todos de la marea, por misérrimos que parezcan; la liga clasifica, y separa a aquellos, para quienes las esperanzas de mejoramiento no son posibles sino probables y a menudo casi realidades.

Los resultados obtenidos por entrambos medios, así como los gastos que uno y otro demandan, no pueden, por tanto equipararse.

No obstante y sólo a título informativo, expondremos los datos siguientes:

Durante los últimos años (1908–1912) fallecieron de tuberculosis, en el Hospital de Infecto-Contagiosos de Montevideo (Hospital Fermín Ferreira), a cargo de la asistencia pública;

1908, 135 fallecidos; 1909, 128; 1910, 243; 1911, 291; 1912, 372; total, 1,169 fallecidos.

Según la memoria de la propia asistencia pública, 1913, la mortalidad de los asilados por tuberculosis, en el referido hospital, durante el año 1912, igualó a la proporción de 25.17 por ciento. Y en cuanto al costo mensual de un enfermo de los asilados, fué el siguiente:

1907–8, $28.85; 1908–9, $24,32; 1909–10, $28.29; 1910–11, $30.55; 1911–12, $31.29.

La Liga Uruguaya contra la Tuberculosis, en cambio, en el solo Departamento de Montevideo, atendió, desde julio de 1902 hasta 31 de diciembre de 1914, en los tres dispensarios que posee, así como en el sanatorio de cura diurna al aire libre, el número de enfermos siguiente con estos resultados:

Número de enfermos asistidos	3,700
(A) Aparentemente curados	910
Proporción, por ciento	24.59
(B) Notablemente mejorados	328
Proporción por ciento	8.86
A+B	1 238
Proporción por ciento	33.45

A este respecto conviene observar que, a pesar, de no admitir en principio la Liga, sino los enfermos curables, en la práctica las excepciones son frecuentes, ingresando en los dispensarios, por razones de caridad, numerosos casos de tuberculosis en los períodos más avanzados de la dolencia. Y por lo que toca a los curados, realmente pueden considerarse así, pues según las prácticas establecidas, se observa durante años el estado ulterior de los dados de alta.

EFICACIA DE LA ACCIÓN POPULAR EN LA ASISTENCIA DEL TUBERCULOSO.

Durante el espacio de tiempo de más de 10 años, hemos asistido día por día a la organización de la liga, desde la fecha en que fué fundada.

Además del mecanismo administrativo y absolutamente nuevo que nos fué dado estudiar y desenvolver, adaptándolo en lo posible al medio ambiente, las exigencias del cargo nos obligaron a estudiar, en sus más insignificantes detalles, la vida del tuberculoso, sus hábitos, sus necesidades, como las de la familia, en las propias moradas. Sólo así nos fué posible darnos cuenta de su número, consiguiendo al mismo tiempo insinuarnos, en el espíritu de los desgraciados, escuchando pacientemente las quejas que la amargura y la miseria provocan. Sólo así, en contacto íntimo con los enfermos, llegamos a inspirar confianza, vale decir, poseer el elemento indispensable para la asistencia y sin el cual ésta resulta absolutamente inútil.

Observadores más autorizados que nosotros, acaso, nieguen el valor de lo que podríamos denominar cura moral del tuberculoso y sostengan que todo debe supeditarse al cumplimiento de una disciplina severa y rígida. Nuestra modesta experiencia, contradice, en absoluto, semejante opinión.

Por desesperante que parezca el estado de muchos enfermos y por decaído que esté el ánimo, de contínuo triste entre los tuberculosos, la presencia de una persona que se interese en semejantes seres, contribuye tanto o más, si cabe, que la virtud de algunos remedios. Y si esa influencia se ejerce de manera inteligentemente consoladora y persuasiva, muy raro es que no se obtengan benéficos resultados.

La acción de la Liga poniendo en contacto íntimo al enfermo, con los encargados de su asistencia, facilitándole los medios de hacer frente a sus necesidades más apremiantes, dándole techo, abrigo y alimentos y enseñándole a precaver del contagio a los seres que le rodean, ha sido fecunda y está llamada, si la organización de sus dispensarios se perfecciona, como es de esperarse, a desempeñar el principal papel en la lucha contra la tuberculosis. Tal es nuestra íntima convicción, abonada con la experiencia de más de diez años de observación paciente y sincera.

Por supuesto que los detalles del procedimiento tienen positivo valor, pues no es lo mismo limitar la asistencia a lo que arrojan el estudio clínico del enfermo, el peso, la amplitud del tórax y el examen de los productos de la expectoración, que ampliarla, visitando su morada, alentando sus cansadas energías y ayudándole en cuanto necesita alivio y consuelo. Todo lo que se diga, en este sentido, resulta pálido, ante la realidad de los hechos. A punto tal que creemos que de la importancia dada a estos numerosos y complejos factores, se debe casi siempre el éxito obtenido, cuando se contemplan y desenvuelven convenientemente.

MORTALIDAD POR TUBERCULOSIS PULMONAR, ABSOLUTA Y PROPORCIONES.

La población del Uruguay, que según el último censo, de 12 de octubre de 1908, sumó la cantidad de 1,042,686 habitantes, ascendió, según cálculos, en 31 de diciembre de 1914, a la de 1,326,506. El aumento referido se debe, en primer término, al aumento migratorio (igual en los años 1909–1913 a la proporción de 24.09 por ciento; y en segundo lugar, al crecimiento vegetativo: (igual en el mismo período, a la proporción de 18.23 por ciento). La población está formada en su totalidad por uruguayos, hijos de los antiguos colonos europeos y por extranjeros; principalmente italianos y españoles.

La proporción de los uruguayos, según el censo de 1908 fué igual a la cifra de 82.62 por ciento y la de extranjeros a la de 17.38 por ciento. Semejantes proporciones no se han alterado sensiblemente en los últimos años.

Durante el período comprendido entre los años 1895–1914, entrambos inclusives, fallecieron de todas las enfermedades, la cantidad de 279,234 individuos, suma que da una proporción media de mortalidad general, en veinte años de observación, igual a 12.18 por 1,000.

Las proporciones medias en los 19 Departamentos en que se halla dividida la República, fueron:

Artigas	15. 46	Paysandú	11. 97
Canelones	10. 32	Río Negro	8. 65
Cerro Largo	12. 44	Rivera	16. 07
Colonia	11. 82	Rocha	11. 37
Durazno	14. 49	Salto	15. 03
Flores	13. 06	San José	11. 93
Florida	11. 56	Soriano	14. 07
Maldonado	10. 81	Tacuarembó	14. 56
Minas	12. 41	Treinta y Tres	11. 57
Montevideo	16. 05		

Durante idéntico período de 20 años fallecieron, de tuberculosis pulmonar en el Uruguay, la cantidad de 21,407 personas, que da la proporción media de 5.38 por ciento, sobre las defunciones generales y la media también proporcional, de 0.69 por cada 1,000 habitantes.

La proporción media de fallecidos de tuberculosis pulmonar, por 100 defunciones, en comparación de las proporciones medias sobre la mortalidad general en los Departamentos fué como sigue:

Artigas	3. 29	Paysandú	8. 41
Canelones	6. 49	Río Negro	4. 56
Cerro Largo	6. 59	Rivera	4. 35
Colonia	6. 68	Rocha	5. 79
Durazno	4. 44	Salto	6. 45
Flores	4. 47	San José	7. 70
Florida	4. 97	Soriano	7. 10
Maldonado	3. 19	Tacuarembó	4. 26
Minas	3. 79	Treinta y Tres	3. 56
Montevideo	11. 55		

Los anteriores guarismos demuestran que, durante los últimos veinte años, en el Uruguay, dentro de una proporción media de la mortalidad general, bastante baja (12.18 por 1,000) la proporción, también media, de fallecidos de tuberculosis pulmonar, por ciento de defunciones generales, tampoco fué elevada pues igualó a la de 5.38 por ciento.

No obstante, estudiando parcial y comparativamente los cuadros estadísticos que hemos formado, es de observar y tenerse en cuenta para ulteriores investigaciones:

Que la cantidad absoluta y proporcional de fallecidos por tuberculosis, en general, ha ido aumentando paulatinamente. Que ese aumento es bastante más sensible en el Departamento de la capital, pudiéndose explicar en parte: por ser de regla el predominio de las afecciones tuberculosas en centros urbanos de población elevada; porque el diagnóstico se establece, donde los servicios médicos abundan, en mejores condiciones y con mayor certeza y porque muchos enfermos del interior acuden a la metrópoli en busca de mejores recursos.

Finalmente: que la proporción de defunciones de tuberculosis, sobre el número de habitantes, en los Departamentos del interior, nunca llegó a la cifra de 2 por 1,000

elevándose sólo la de Montevideo (cuya media fué de 1.85 en 20 años) hasta 2.13 por 1,000, en 1911, 2.22 en 1912, y 2.25 en 1914. La proporción media, en el Uruguay, en los últimos 20 años fué de 0.69 por 1,000 habitantes.

RESUMEN.

La lucha contra la tuberculosis en el Uruguay cuenta con elementos diversos bastante bien organizados en su conjunto. En el interior, como en la capital, la asistencia se lleva a la práctica con el concurso de los Hospitales que dependen de la Asistencia Pública y el de las Ligas. Estas últimas tienden a desarrollarse cada vez más, con positivo provecho.

La declaración obligatoria de la tuberculosis existe en vigencia desde 1896. La práctica de la desinfección se lleva a cabo regularmente en la Capital y tiende a regularizarse en el interior.

El aislamiento del enfermo se realiza, en Montevideo, en los pabellones que la administración posee y en algunos departamentos, como el del Salto, en las instalaciones de las Ligas.

Además de esos instrumentos de cura y preservación, deben considerarse como factores coadyuvantes: los asilos maternales (tres en Montevideo); la Copa de leche (una principal con siete sucursales); las Colonias de vacaciones, concursos de lactantes; funciones del cuerpo médico escolar; Casa de maternidad; diversas leyes de protección a la infancia, a las madres, defensa de menores, etc., Hospital de niños, casa cuna, y servicios interno y externo de huérfanos atendidos en el hospital con nodriza y alimentados artificialmente.

La vigilancia sanitaria de los animales se lleva a cabo en condiciones regulares, organizada convenientemente por la Dirección de Ganadería y por la Inspección Veterinaria.

En el espacio de los últimos 20 años, la mortalidad general y por tuberculosis, en el Uruguay, llegó a las cifras absolutas y proporcionales siguientes:

Años 1895 a 1914 (inclusives): Mortalidad general, 279,234; proporción media por mil, 12.18; mortalidad por tuberculosis pulmonar, 21,407; proporción media por mil habitantes, 0.69; proporción media por cien defunciones, 5.38.

Años, población, mortalidad general, tuberculosis pulmonar y proporciones, 1895–1914.

DEPARTAMENTO DE ARTIGAS.

Años.	Población.	Mortalidad general.	Proporción media por 1,000 habitantes.	Mortalidad por tuberculosis pulmonar.	Proporción media por 1,000 habitantes.	Proporción media por 100 defunciones generales.
1895	20,351	427	20.98	7	0.34	1.63
1896	21,174	409	19.31	6	.28	1.46
1897	21,716	349	16.06	13	.59	3.72
1898	22,309	379	16.98	18	.80	4.74
1899	22,904	275	12.00	4	.17	1.45
1900	26,004	379	14.57	10	.38	2.63
1901	27,001	426	15.77	11	.40	2.58
1902	27,663	627	23.66	17	.61	2.71
1903	28,354	469	16.59	11	.38	2.34
1904	28,971	242	8.35	4	.14	1.65
1905	30,574	410	13.41	7	.22	1.70
1906	32,805	471	14.35	11	.33	2.33
1907	36,439	499	13.69	11	.30	2.20
1908	27,076	445	16.43	11	.40	2.47
1909	28,719	530	18.45	13	.45	2.45
1910	29,622	539	18.19	20	.67	3.71
1911	31,380	543	17.30	38	1.21	6.99
1912	33,470	459	13.71	27	.80	5.88
1913	35,151	445	12.65	18	.51	4.04
1914	36,340	461	12.68	32	.88	6.94
	.....	8,784	15.46	289	.50	3.29

Años, población, mortalidad general, tuberculosis pulmonar y proporciones, 1895–1914—Continúa.

DEPARTAMENTO DE CANELONES.

Años.	Población.	Mortalidad general.	Proporción media por 1,000 habitantes.	Mortalidad por tuberculosis pulmonar.	Proporción media por 1,000 habitantes.	Proporción media por 100 defunciones generales.
1895	64,575	1,020	15.79	46	0.71	4.50
1896	66,877	883	13.20	46	.68	5.20
1897	68,553	944	13.47	55	.80	5.82
1898	79,468	979	13.89	72	1.02	7.35
1899	72,618	890	12.25	46	,63	5.16
1900	83,143	962	11.57	38	.45	3.95
1901	86,735	844	9.73	38	.43	4.50
1902	88,793	829	9.33	61	.68	7.35
1903	90,851	848	9.33	44	.48	5.18
1904	92,877	822	8.85	51	.54	6.20
1905	94,776	857	9.04	73	.77	8.51
1906	98,014	897	9.15	64	.65	7.13
1907	100,560	1,021	10.15	74	.73	7.24
1908	88,581	853	9.62	66	.74	7.73
1909	91,556	863	9.42	78	.85	9.03
1910	94,521	1,024	10.83	68	.71	6.64
1911	97,719	926	9.47	80	.81	8.63
1912	100,981	1,029	10.19	67	.66	6.51
1913	104,391	893	8.55	60	.57	6.71
1914	107,068	820	7.65	55	.51	6.70
	.....	18,204	10.32	1,182	.67	6.49

DEPARTAMENTO DE CERRO LARGO.

1895	28,795	423	14.69	10	0.34	2.36
1896	29,564	409	13.83	20	.67	4.88
1897	29,909	379	12.67	32	1.06	8.44
1898	30,743	408	13.27	32	1.04	7.84
1899	31,666	333	10.51	25	.78	7.50
1900	36,396	386	10.60	37	1.01	9.58
1901	37,236	411	11.03	27	.72	6.56
1902	37,979	472	12.42	29	.76	6.14
1903	33,825	413	10.63	32	.82	7.74
1904	39,234	146	3.72	12	.30	8.21
1905	40,437	549	13.57	27	.66	4.91
1906	4 ,401	590	13.91	39	.91	6.61
1907	43,787	595	13.58	26	.59	4.36
1908	45,103	678	15.03	48	1.06	7.07
1909	46,404	733	15.79	42	.90	5.72
1910	47,645	590	12.38	36	.75	6.10
1911	49,307	606	12.29	38	.77	6.27
1912	51,025	688	13.48	49	.96	7.12
1913	52,794	680	12.88	48	.90	7.05
1914	54,005	635	11.75	59	1.09	9.29
	.....	10,124	12.44	668	.82	6.59

DEPARTAMENTO DE COLONIA.

1895	38,031	555	14.59	36	0.94	6.48
1896	39,703	535	13.47	40	1.00	7.47
1897	41,021	668	16.28	34	.82	5.08
1898	42,128	687	16.30	44	1.04	6.40
1899	43,361	570	13.14	40	.92	7.01
1900	50,275	691	13.74	47	.93	6.80
1901	51,563	643	12.47	38	.73	5.90
1902	53,223	604	11.34	32	.60	5.29
1903	54,357	658	12.10	47	.86	7.14
1904	55,686	585	10.50	34	.61	5.81
1905	56,335	590	10.47	45	.79	7.62
1906	59,000	686	11.62	46	.77	6.70
1907	61,630	659	10.69	46	.74	6.98
1908	55,167	634	11.49	38	.68	5.99
1909	58,097	660	11.36	49	.84	7.42
1910	60,442	860	14.22	46	.76	5.34
1911	63,732	711	11.15	63	.98	8.86
1912	67,151	693	10.32	53	.78	7.64
1913	71,572	6'6	8.73	45	.62	7.20
1914	74,458	657	8.82	44	.59	6.69
	.....	12,971	11.82	867	.79	6.68

Años, población, mortalidad general, tuberculosis pulmonar y proporciones, 1895-1914—continúa.

DEPARTAMENTO DE DURAZNO.

Años.	Población.	Mortalidad general.	Proporción media por 1,000 habitantes.	Mortalidad por tuberculosis pulmonar.	Proporción media por 1,000 habitantes.	Proporción media por 100 defunciones generales.
1895	28,793	608	21.11	23	0.79	3.78
1896	29,525	680	23.03	22	.74	3.23
1897	30,064	638	21.22	26	.83	3.91
1898	30,732	639	20.79	17	.55	2.66
1899	31,646	536	16.93	17	.53	3.17
1900	37,141	571	15.37	27	.72	4.72
1901	38,111	488	12.80	13	.34	2.66
1902	38,964	558	14.32	18	.46	3.22
1903	39,963	526	13.15	19	.47	3.61
1904	40,548	508	12.52	22	.54	4.33
1905	41,477	470	11.33	31	.74	6.59
1906	43,413	668	15.38	32	.73	4.79
1907	44,690	765	17.11	22	.49	2.87
1908	42,784	592	13.83	27	.63	4.56
1909	44,268	552	12.46	31	.70	5.61
1910	45,628	593	12.99	27	.59	4.55
1911	47,253	608	12.86	47	.99	7.73
1912	48,871	717	14.67	32	.65	4.46
1913	50,690	549	10.83	34	.67	6.19
1914	51,737	565	10.92	40	.77	7.07
	.....	11,831	14.49	526	.64	4.44

DEPARTAMENTO DE FLORES.

1895	14,818	202	13.63	12	0.80	5.94
1896	15,134	224	14.80	5	.33	2.23
1897	15,390	210	13.64	7	.45	3.33
1898	15,753	186	11.80	17	1.07	9.13
1899	16,063	188	11.70	13	.80	6.91
1900	15,874	183	11.52	14	.88	7.65
1901	16,180	234	14.46	9	.55	3.84
1902	16,482	245	14.86	13	.78	5.30
1903	16,805	207	12.31	9	.53	4.34
1904	17,086	226	13.22	8	.46	3.53
1905	17,355	263	15.15	4	.23	1.52
1906	18,868	224	11.87	6	.31	2.67
1907	19,853	238	11.98	6	.30	2.52
1908	16,376	258	15.75	7	.42	2.71
1909	17,233	246	14.27	7	.40	2.84
1910	18,080	250	13.82	11	.60	4.40
1911	19,030	242	12.71	13	.68	5.37
1912	20,131	254	12.61	14	.69	5.51
1913	21,161	257	12.14	15	.70	5.83
1914	21,562	224	10.38	14	.64	6.25
	.....	4,561	13.06	204	.58	4.47

DEPARTAMENTO DE FLORIDA.

1895	34,178	466	13.63	22	0.64	4.72
1896	35,134	514	14.62	27	.74	5.25
1897	36,024	469	13.01	36	.99	7.67
1898	36,871	506	13.72	29	.78	5.73
1899	37,920	461	12.15	23	.60	4.98
1900	44,054	484	10.98	17	.38	3.51
1901	45,248	444	9.81	28	.61	6.30
1902	46,344	493	10.63	33	.71	6.69
1903	47,493	566	11.91	29	.61	5.12
1904	48,454	482	9.94	13	.26	2.69
1905	49,666	570	11.47	19	.38	3.33
1906	52,018	572	10.99	34	.65	5.94
1907	53,656	735	13.69	39	.72	5.30
1908	45,887	582	12.68	22	.47	3.78
1909	47,553	511	10.74	25	.52	4.89
1910	49,229	565	11.47	30	.60	5.30
1911	51,202	569	11.11	31	.60	5.44
1912	53,158	627	11.79	25	.47	3.98
1913	55,432	454	8.19	25	.45	5.50
1914	56,917	525	9.22	20	.35	3.80
	.....	10,595	11.56	527	.57	4.97

Años, población, mortalidad general, tuberculosis pulmonar y proporciones, 1895–1914—Continúa.

DEPARTAMENTO DE MALDONADO.

Años.	Población.	Mortalidad general.	Proporción media por 1,000 habitantes.	Mortalidad por tuberculosis pulmonar.	Proporción media por 1,000 habitantes.	Proporción media por 100 defunciones generales.
1895	21,907	231	11.45	16	0.73	6.92
1896	22,425	460	20.51	10	.44	2.17
1897	23,086	248	10.74	13	.56	5.24
1898	23,835	304	12.71	15	.62	4.93
1899	24,483	270	11.02	14	.57	5.18
1900	26,439	305	11.53	6	.22	1.96
1901	27,035	280	10.35	7	.25	2.50
1902	27,729	277	9.98	8	.28	2.88
1903	28,304	347	12.25	8	.28	2.30
1904	28,968	261	9.00	6	.20	2.29
1905	29,631	293	9.88	3	.10	1.02
1906	31,419	307	9.77	10	.31	3.25
1907	32,697	295	9.02	10	.30	3.38
1908	29,276	333	11.37	10	.34	3.00
1909	30,588	324	10.59	7	.22	2.16
1910	31,818	348	10.93	8	.25	2.29
1911	33,168	381	11.48	11	.33	2.88
1912	34,704	367	10.57	19	.54	5.17
1913	36,306	314	8.64	11	.30	3.50
1914	37,125	339	9.13	9	.24	2.65
	.....	6,284	10.81	201	.34	3.19

DEPARTAMENTO DE MINAS.

1895	26,702	418	15.61	18	0.67	4.30
1896	27,604	528	19.48	13	.47	2.40
1897	28,401	422	14.85	17	.59	4.02
1898	29,287	445	15.19	16	.54	3.59
1899	30,369	446	14.68	13	.42	2.91
1900	36,085	529	14.65	17	.47	3.21
1901	37,152	513	13.80	13	.34	2.53
1902	38,155	545	14.28	13	.34	2.38
1903	39,306	525	13.35	16	.40	3.04
1904	40,269	429	10.65	12	.29	2.79
1905	41,426	540	13.03	20	.48	3.70
1906	43,727	620	14.17	36	.82	5.80
1907	45,334	726	16.01	36	.79	4.95
1908	51,713	583	11.27	22	.42	3.77
1909	53,399	595	11.14	40	.74	6.72
1910	55,097	617	11.19	21	.38	3.40
1911	57,036	641	11.23	23	.40	3.58
1912	59,229	581	9.80	17	.28	2.92
1913	61,479	512	8.32	16	.26	3.12
1914	62,920	522	8.29	29	.46	5.55
	.....	10,737	12.41	408	.47	3.79

DEPARTAMENTO DE MONTEVIDEO.

1895	258,990	3,891	15.02	432	1.66	11.10
1896	261,182	3,995	15.29	477	1.82	11.94
1897	264,838	3,986	15.05	455	1.71	11.41
1898	264,704	3,980	15.03	381	1.43	9.57
1899	265,572	3,902	14.65	397	1.49	10.17
1900	268,334	4,267	15.95	482	1.79	11.29
1901	273,665	4,374	15.98	494	1.80	11.29
1902	276,034	4,466	16.17	487	1.76	10.90
1903	282,689	4,530	16.02	544	1.92	12.00
1904	289,018	4,638	16.04	554	1.91	11.94
1905	298,533	4,402	14.74	516	1.72	11.72
1906	307,482	5,042	16.39	584	1.89	11.58
1907	309,904	4,980	16.07	563	1.81	11.30
1908	313,016	4,822	15.40	560	1.78	11.61
1909	321,224	5,466	17.01	595	1.85	10.88
1910	329,888	6,162	18.67	658	1.99	10.67
1911	338,353	5,829	17.22	722	2.13	12.38
1912	355,017	6,336	17.84	790	2.22	12.46
1913	374,005	5,824	15.57	644	1.74	11.06
1914	375,135	5,896	15.71	846	2.25	14.34
	.....	96,788	16.06	11,181	1.85	11.55

Años, población, mortalidad general, tuberculosis pulmonar y proporciones, 1895–1914—Continúa.

DEPARTAMENTO DE PAYSANDÚ.

Años.	Población.	Mortalidad general.	Proporción media por 1,000 habitantes.	Mortalidad por tuberculosis pulmonar.	Proporción media por 1,000 habitantes.	Proporción media por 100 defunciones generales.
1895	36,448	477	13.08	46	1.26	9.64
1896	38,440	590	15.34	28	.72	4.74
1897	40,431	625	15.45	47	1.16	7.52
1898	42,911	581	13.63	36	.83	6.19
1899	44,344	491	11.07	23	.51	4.68
1900	43,121	517	11.98	36	.83	6.96
1901	44.411	507	11.41	41	.92	8.08
1902	45,655	576	12.61	39	.85	6.77
1903	47,086	554	11.76	39	.82	7.03
1904	48,149	425	8.82	32	.66	7.52
1905	49,784	517	10.38	56	1.12	10.83
1906	52,398	622	11.87	57	1.08	9.16
1907	54,097	608	11.23	53	.97	8.71
1908	38,883	587	15.09	38	.97	6.47
1909	42,143	543	12.88	68	1.61	12.52
1910	45,127	552	12.23	54	1.19	9.78
1911	48,419	698	14.41	76	1.56	10.88
1912	52,038	545	10.47	50	.96	9.17
1913	57,146	581	10.16	63	1.10	10.84
1914	60,512	561	9.27	57	.94	10.16
	.....	11,157	11.97	939	1.00	8.41

DEPARTAMENTO DE RÍO NEGRO.

1895	20,771	209	10.06	11	0.52	5.26
1896	22,199	252	11.35	14	.63	5.55
1897	24,369	246	10.09	11	.45	4.47
1898	25,989	219	8.42	11	.42	5.02
1899	28,219	229	8.11	11	.38	4.80
1900	21,202	201	9.48	7	.33	3.48
1901	23,127	244	10.55	16	.69	6.55
1902	25,157	222	8.82	8	.31	3.60
1903	28,133	222	7.89	12	.42	5.40
1904	31,103	210	6.75	9	.28	4.28
1905	33,316	240	7.20	10	.30	4.16
1906	36,925	299	8.09	6	.16	2.00
1907	39,667	244	6.15	14	.35	5.73
1908	20,565	237	11.52	13	.63	5.48
1909	23,276	221	10.18	8	.34	3.37
1910	25,452	236	8.68	9	.35	4.07
1911	27,622	263	10.35	12	.43	4.19
1912	29,631	252	8.87	6	.20	2.28
1913	31,907	237	7.89	10	.31	3.96
1914	33,529	246	7.33	20	.59	8.13
	.....	4,779	8.65	218	.39	4.56

DEPARTAMENTO DE RIVERA.

1895	17,938	415	23.13	4	0.22	0.96
1896	18,514	390	21.06	13	.70	3.33
1897	18,767	209	11.13	16	.85	7.65
1898	19,233	324	16.84	16	.83	4.93
1899	19,820	281	14.17	18	.90	6.40
1900	24,792	368	14.84	15	.60	4.07
1901	25,349	329	12.97	6	.23	1.82
1902	25,907	432	16.67	7	.27	1.62
1903	26,360	416	15.78	11	.41	2.64
1904	26,556	179	6.74	8	.30	4.46
1905	27,212	461	16.94	13	.47	2.81
1906	28,831	576	19.97	19	.65	3.29
1907	30,051	470	15.64	23	.76	4.89
1908	36,063	500	13.86	31	.85	6.20
1909	37,146	596	16.04	31	.83	5.20
1910	38,227	521	13.62	26	.68	4.99
1911	39,413	793	20.12	30	.76	3.78
1912	41,030	710	17.20	27	.65	3.80
1913	42,503	679	15.97	42	.98	6.18
1914	43,342	625	14.42	48	1.10	7.68
	.....	9,274	16.07	404	.70	4.35

Años, población, mortalidad general, tuberculosis pulmonar y proporciones, 1895–1914—Continúa.

DEPARTAMENTO DE ROCHA.

Años.	Población.	Mortalidad general.	Proporción media por 1,000 habitantes.	Mortalidad por tuberculosis pulmonar.	Proporción media por 1,000 habitantes.	Proporción media por 100 defunciones generales.
1895	24,619	272	11.04	19	0.77	6.98
1896	25,251	416	16.47	20	.79	4.80
1897	25,976	316	12.16	10	.38	3.16
1898	26,704	354	13.25	16	.59	4.51
1899	27,549	298	10.81	10	.36	3.35
1900	29,550	326	11.03	14	.47	4.29
1901	30,428	309	10.15	14	.46	4.53
1902	31,167	372	11.93	22	.70	5.91
1903	32,010	437	13.65	15	.46	3.43
1904	32,698	328	10.03	19	.58	5.79
1905	33,556	388	11.56	21	.62	5.41
1906	35,582	381	10.70	25	.70	6.56
1907	37,020	415	11.21	19	.51	4.57
1908	34,543	404	11.69	26	.75	6.43
1909	36,023	386	10.71	27	.74	6.99
1910	37,438	412	10.99	27	.72	6.55
1911	39,038	408	10.45	29	.74	7.10
1912	40,705	447	10.98	28	.68	6.26
1913	42,351	474	11.19	41	.96	8.64
1914	43,309	431	9.95	37	.85	8.58
	.....	7,574	11.37	439	.65	5.79

DEPARTAMENTO DE SALTO.

1895	35,881	631	17.58	29	0.80	4.59
1896	36,801	735	19.97	37	1.00	5.03
1897	37,586	608	16.17	50	1.33	8.25
1898	38,329	681	17.76	50	1.30	7.34
1899	39,451	560	14.19	46	1.16	8.21
1900	44,675	634	14.19	37	0.82	5.83
1901	45,754	631	13.79	39	0.85	6.18
1902	46,793	763	16.30	50	1.06	6.55
1903	47,615	912	19.15	52	1.09	5.70
1904	48,326	554	11.46	46	0.95	8.30
1905	49,646	655	13.19	25	0.50	3.81
1906	51,661	784	15.17	44	0.85	5.61
1907	53,154	877	16.49	53	0.99	6.04
1908	46,801	749	16.00	39	0.83	5.20
1909	48,656	753	15.47	52	1.06	6.90
1910	51,002	783	15.35	39	0.74	4.98
1911	54,159	788	14.54	51	0.94	6.47
1912	56,875	799	14.04	58	1.01	7.25
1913	60,175	744	12.36	73	1.21	9.81
1914	66,493	789	11.88	62	0.93	7.85
	.....	14,430	15.03	982	0.97	6.45

DEPARTAMENTO DE SAN JOSÉ.

1895	32,605	474	14.53	41	1.25	8.64
1896	33,545	489	14.57	31	0.92	6.33
1897	34,441	510	14.80	50	1.45	9.80
1898	35,286	589	16.69	69	1.38	8.31
1899	36,354	516	14.19	48	1.32	9.30
1900	41,055	640	15.58	36	0.87	5.62
1901	42,181	489	11.59	26	0.61	5.31
1902	43,199	496	11.48	37	0.85	7.45
1903	44,257	514	11.61	40	0.90	7.78
1904	45,353	472	10.40	38	0.83	8.05
1905	46,368	530	11.43	29	0.62	5.47
1906	48,671	541	11.11	47	0.96	8.68
1907	50,304	615	12.22	48	0.95	7.80
1908	46,810	571	12.19	44	0.93	7.70
1909	48,400	585	12.08	52	1.07	8.88
1910	50,034	615	12.29	41	0.81	6.66
1911	51,785	626	12.08	46	0.88	7.34
1912	53,698	533	9.92	31	0.57	5.81
1913	55,673	490	8.80	52	0.93	10.61
1914	57,011	436	7.64	41	0.71	9.40
	.....	10,731	11.93	827	0.91	7.70

Años, población, mortalidad general, tuberculosis pulmonar y proporciones, 1895–1914—Continúa.

DEPARTAMENTO DE SORIANO.

Años.	Población.	Mortalidad general.	Proporción media por 1,000 habitantes.	Mortalidad por tuberculosis pulmonar.	Proporción media por 1,000 habitantes.	Proporción media por 100 defunciones generales.
1895	35,214	516	14.65	40	1.13	7.75
1896	35,972	481	13.37	44	1.22	9.14
1897	36,309	694	19.07	38	1.04	5.47
1898	37,451	483	12.89	40	1.06	8.28
1899	38,377	527	13.73	41	1.06	7.77
1900	38,047	629	16.53	31	.81	4.92
1901	38,851	616	15.85	45	1.15	7.30
1902	39,861	507	12.71	29	.72	5.71
1903	40,886	603	14.74	46	1.12	7.62
1904	41,768	573	13.71	45	1.07	7.85
1905	42,535	584	13.72	35	.82	5.99
1906	44,487	627	14.09	49	1.10	7.81
1907	46,386	638	13.75	57	1.22	8.93
1908	39,977	605	15.13	44	1.10	7.27
1909	41,617	613	14.72	36	.86	5.87
1910	42,758	747	17.47	45	1.05	6.02
1911	44,720	641	14.33	48	1.07	7.48
1912	46,910	528	11.25	38	.81	7.19
1913	49,593	547	11.02	56	1.12	10.23
1914	51,413	568	11.04	37	.71	6.51
	.....	11,727	14.07	844	1.01	7.19

DEPARTAMENTO DE TACUAREMBO.

1895	26,525	561	21.14	29	1.09	5.16
1896	27,373	538	19.65	19	.69	3.53
1897	27,929	461	16.50	18	.64	3.90
1898	28,707	447	15.57	23	.80	5.14
1899	29,602	387	13.07	20	.67	5.16
1900	37,851	470	12.41	15	.39	3.19
1901	38,789	506	13.04	15	.38	2.96
1902	39,569	641	16.19	31	.78	4.83
1903	40,412	618	15.29	29	.71	4.69
1904	40,680	303	7.44	12	.29	3.96
1905	42,104	709	16.83	12	.28	1.69
1906	44,173	748	16.93	36	.81	4.81
1907	45,580	719	15.77	43	.94	5.98
1908	47,418	664	14.00	24	.50	3.61
1909	48,787	697	14.28	31	.63	4.44
1910	50,104	709	14.15	30	.59	4.23
1911	51,505	870	16.89	37	.71	4.25
1912	53,169	759	14.27	29	.54	3.82
1913	55,285	650	11.75	21	.56	4.76
1914	56,438	661	11.71	33	.58	4.99
	.....	12,118	14.56	517	.62	4.26

DEPARTAMENTO DE TREINTA Y TRES.

1895	21,732	314	14.44	14	0.64	4.45
1896	22,221	250	11.25	7	.31	2.80
1897	22,615	240	10.60	4	.17	1.66
1898	23,089	261	11.30	4	.17	1.53
1899	23,567	289	12.26	9	.38	3.11
1900	25,036	336	13.42	7	.27	2.08
1901	25,800	216	8.37	1	.03	.46
1902	26,369	314	11.90	8	.30	2.54
1903	27,221	306	11.24	1	.03	.32
1904	27,722	131	4.72	3	.10	2.29
1905	28,495	339	11.89	5	.17	1.47
1906	30,193	428	14.17	15	.49	3.50
1907	31,360	462	14.73	16	.51	3.46
1908	29,154	324	11.11	13	.44	4.01
1909	30,318	359	11.84	12	.39	3.34
1910	31,436	407	12.94	17	.54	4.17
1911	32,897	386	11.73	21	.63	5.44
1912	34,650	410	11.83	24	.69	5.85
1913	36,284	404	11.13	28	.77	6.93
1914	37,192	389	10.45	25	.67	6.42
	.....	6,565	11.57	234	.41	3.56

Resumen de la población, mortalidad general, tuberculosis pulmonar y proporciones, por Departamentos y años, 1895–1914.

Departamentos.	Población media.	Mortalidad general.	Proporción media por 1,000 habitantes.	Mortalidad media por tuberculosis pulmonar.	Proporción media por 1.000 habitantes.	Proporción media por 100 funciones generales.
Artigas	28,396	3,784	15.46	269	0.50	3.29
Canelones	88,182	18,204	10.32	1,182	.67	6.49
Cerro Largo	40,662	10,124	12.44	668	.82	6.59
Colonia	54,843	12,971	11.82	867	.79	6.66
Durazno	40,815	11,831	14.49	526	.64	4.44
Flores	17,461	4,561	13.06	204	.58	4.47
Florida	45,821	10,595	11.56	527	.57	4.97
Maldonado	29,047	6,284	10.81	201	.34	3.19
Minas	43,237	10,757	12.41	406	.47	3.79
Montevideo	301,379	96,788	16.05	11,181	1.85	11.55
Paysandú	46,577	11,157	11.97	939	1.00	8.41
Río Negro	27,607	4,779	8.65	218	.39	4.56
Rivera	28,852	9,274	16.07	404	.70	4.35
Rocha	33,278	7,674	11.37	439	.65	5.79
Salto	47,991	14,430	15.03	932	.97	6.45
San José	44,951	10,731	11.93	827	.91	7.70
Toriano	41,659	11,727	14.07	844	1.01	7.19
Tacuarembo	41,600	12,118	14.56	517	.62	4.26
Treinta y Tres	28,367	6,565	11.57	234	.41	3.56
Total	.....	279,234	12.18	21,407	.69	5.38

"A TOOTH IS MORE VALUABLE THAN A DIAMOND."[1]

By FELIPE GALLEGOS,

Secretary of the Dental Faculty of Costa Rica.

"In the lower jaw," said Sancho, "your lordship has only two molars and a half; and above neither a half nor a single one, as all is even as the palm of the hand." "Pity on me!" said Don Quixote, hearing the sad news that his squire gave him, "that I would prefer to have lost an arm, excepting the one with which I sway my sword; because know it, Sancho, a mouth without teeth is as bad as a mill without stone; and so a tooth is more valuable than a diamond."—From the Quixote of Cervantes.

This lecture on oral hygiene has been written so as to help all teachers of the Costa Rican schools in their efforts to promote hygiene measures of all kinds. My aim has been to make it clear to all children, avoiding technical names, and treating in detail the more important questions related to the subject.

Among the best and most important laurels of civilization are those in which scientific research finds something to avoid pain or to prevent the diseases that make life short or unbearable. For such reason civilized countries make hygiene something like a worship, and to insure efficiency they give it the support and force of law.

The first sociological step to prevent tuberculosis and most infectious diseases is oral hygiene. Children have seen at public places billboards which say "It is prohibited to spit on the floor, since tuberculosis is propagated thereby." You see now how necessary for the general health is hygiene of the mouth, and why it is so important that dentists become apostles of it, teaching habits of cleanliness to the rising generation.

[1] Conference on Oral Hygiene for the Schools of Costa Rica.

The care of the teeth is necessary at all ages, but the most critical period is between the sixth and fifteenth years of age. It is during that period of life that the temporary teeth are shed and the permanent ones appear, with the exception of the 20-year molars. In childhood, also, the teeth are more prone to caries, as they are very soft. Children also are more inclined to neglect their teeth in this growing age. Many of them are also very poor and can have neither good food nor healthy homes.

The necessity of having healthy teeth is evident. To enjoy good health it is necessary to digest well the food that is eaten, and that can not be accomplished if the food is not masticated slowly and strongly. The food must be finely ground and mixed with the saliva so that in reaching the stomach it is in condition of being immediately digested and assimilated. We must bear in mind the axiom that says: That it is not the quantity of food eaten, but the quantity assimilated that is of value and gives strength to the body.

Parents ought to see that their children acquire the habit of cleaning their teeth before going to bed, beginning when the little ones are 3 years old, because when the temporary teeth begin to decay and give them pain in the act of mastication the children acquire the habit of chewing with the front teeth only and swallow the food unprepared. The jaws, for lack of exercise, do not develop well and properly so as to accommodate the larger permanent teeth. That lack of exercise in mastication and the premature extractions of the temporary teeth are the principal cause of so many irregularities in children's mouths.

When 3 years of age the child has 20 pieces in its mouth. These begin to change at the age of 6, but before beginning to change, and behind the milk molar teeth, the first permanent molar makes its appearance, say between the fifth and sixth years of age. This is a most important fact in the care of the children's teeth, as unhappily 50 per cent of them lose those teeth because their parents confuse them with the temporary and let them decay beyond recovery, or take the child to some ignorant person who instead of saving it extracts it, causing an irreparable loss to the little one.

I do not exaggerate the facts, and it is enough to say that the first permanent molar is the largest of all. Its premature extraction makes the others appear in a wrong place, many times inclined forward.

There are few things so interesting as the human dental arch. Only man has his set of teeth arranged in a continuous row without spaces between them, and articulating perfectly with its fellows on the opposite jaw. And it is that wonderful harmony that is broken by the ignorant who extract a tooth that could be saved, to be useful for a life time.

After the six-year molars, come the second at the age of 12, and the wisdom at 20; six pieces more in each jaw, making in all 32 pieces in the mouth of an adult person.

Children should observe, in cleaning the mouth, the following simple procedure: Immediately after eating it is a good practice to use (not to abuse) a quill toothpick, or floss silk, to take off meat fibres and the like which may become pressed between the teeth. Pins and matches should never be used for picking the teeth. Matches sometimes have large amounts of poison which have caused violent inflammations, many times with very serious complications. Select a good toothbrush, neither too soft nor too hard, and use it slowly, with a movement somewhat downwards, in the upper teeth, and somewhat upward in the lower ones; in using the brush only horizontally as it is generally done, you can not clean the spaces so well, and the gums suffer. Use the brush on the inside as well as on the outside, all over the teeth. It is convenient to clean the teeth after each meal, but absolutely necessary to do it at night before retiring, as that is the time when caries progress more. The child that does not clean his mouth at that time will be always suffering with bad teeth. If cold water is unpleasant, use tepid water for the cleaning. It is good to use a tooth powder often, to avoid stains; the tooth soaps are not to be recommended, as they

make the brush too soft. Use what your dentist recommends for you, but never use dentrifices of unknown formulæ, as they may contain deleterious substances. The S. S. White Dental Manufacturing Co. makes good preparations. I use to a great extent listerine, and find that is about all that is necessary.

The toothbrush must be washed well and made dry with a clean towel every time it is used—otherwise it will be a focus of infection; then keep the brush in a clean place where it can not be confused with any other.

An English proverb says: "Cleanliness is next to godliness." The breath of a young girl of 15, who has always taken care of her teeth, is sweet, and when she smiles, shows, as the poets say, "two rows of pearls in a ruby case." But if it has been otherwise; if there has been ignorance and neglect, then the awful caries, working little by little, will be found making ravages; because the residues of food accumulate and become decomposed, forming acids which attack the inorganic portion of the teeth; and then also millions of microbes live and multiply, and attack the organic portion of the same; and so caries multiply and progress, destroying the enamel first, then the dentine, till the destruction reaches the pulp, or nerve of the teeth; calcareous matter forms; the gums become spongy and purulent; the breath becomes fetid, and the patient, in eating, contaminates his food with those microbes, pus, and decomposed matter; and then will soon come the excruciating pains, the neuralgias, the stomatitis, the tonsilitis, etc., because a mouth in such state, so lamentable, is a favorite breeding place for tuberculosis, for diphptheria, and all infectious diseases.

From what has been said, it is seen clearly that the parent that takes due care of the health of his children must see that they acquire the habit of cleanliness at an early date; and must also take them frequently to the family dentist to have their mouth examined; the temporary as well as the permanent teeth, and not wait till pain, as a protest for the neglect, obliges the forgetful father to take his boy to the dental office when it is generally too late to save the aching tooth.

In the relations between the client and the dentist each receive something: the client the professional services; the dentist some money. When the operation has been performed well, it is the client who receives the better portion. Good dentists give free and timely advice, which many times is worth ten times the amount paid for an operation.

As a contrast, there comes to my mind a case of a young man, 20 years old, who went to see a surgeon-dentist to have his teeth examined. The surgeon found enough to be done, the cost of which he put at a reasonable sum. The young fellow then went to see a quack, who for half price extracted all his upper teeth and made him an artificial substitute. But the fool looked very happy, showing on his hand a very valuable ring with precious stones as an adornment of his body—that same body that had been mutilated by a false idea of economy. Oh, if that young man with such a narrow mind had been able to comprehend the great truth said in the immortal phrase of Don Quixote, "A tooth is more valuable than a diamond," he would have saved his teeth instead of using diamonds on his fingers.

The light of better times is beginning to shine, and the more cultured nations have begun a generous and eminently altruistic movement by founding free clinics to care for the teeth of poor children who attend the schools. Here in Costa Rica there are many dentists who want to begin a similar movement; and it is to be hoped that the good idea will soon be a reality. In conclusion, all children should be made to understand two fundamental things: (1) That without good teeth it is not possible to have good health, and for that reason each tooth is worth, in reality, more than a diamond; (2) that constant care and cleanliness of the mouth is indispensable to keep the teeth in good condition, and at the same time it is the means to prevent tuberculosis and most contagious diseases.

The CHAIRMAN. Dr. Carter will open the discussion on the general topic of this session.

Dr. CARTER. I have only a few remarks to make on what Dr. Sagárnaga read. I suppose that the great height of Bolivia and the high clear mountain atmosphere would have made it fairly free from tuberculosis, but there are some factors that I myself had not appreciated. Among others is the large Indian population. I understood him to say that there were from one to three million Indians in the country, who, in the first place, have a racial susceptibility to tuberculosis, although they are naturally out-of-door people; that when they are housed they are very much crowded together so that infection among them is very great; that they live in a good deal of squalor, have what we would consider insufficient food, and it is among them that tuberculosis so greatly extends.

Again he calls attention to what we in North America and Europe have not to contend with. Our heights are never sufficient for mal de montaña. The higher we get, the better we like it. On the other hand, as I have said, the heights in Bolivia are so great that he speaks of the bad effect of the siroche on the heart.

Those are points that I had never thought of, but surely are very important.

Dr. SAGÁRNAGA. Dr. Solano says in his paper that the Indians in Bolivia, rather contrary to the native Indians in North America, are not susceptible to tuberculosis. He says he does not find any cases among the Indians, and that the ones to contract tuberculosis are the middle-class alcoholics. He has seen Indians working as high as 15,000 feet in the mines, and among them there are no cases of tuberculosis, notwithstanding the fact that their food is very poor, as they eat practically nothing but cocoa leaves.

The CHAIRMAN. I may say that my own experience with the American Indian 15 or 20 years ago showed me that they were singularly free from tuberculosis until they were actually put into habitations unfit for human beings. At the time I knew them in their native state in the States of Nevada, Oregon, and Idaho, and in northern California, occupying their native tepees with copious and ample ventilation, I never saw a case of tuberculosis among those North American Indians. That is based on an experience of several trips I made to that country. I knew of no cases of tuberculosis among them until the housing movement was begun and they were encouraged to build houses. On account of necessary economy the houses were small, about 12 by 15 feet, with two or three small windows perhaps and a door, and a whole family congregated in these little holes, with deficient ventilation and deficient sunlight. There was a development of tuberculosis coincident with this change in their mode of housing. I do not know of any other factor that predisposes one to the same extent to that condition, because we know that bad housing conditions favor the development of tuberculosis and other so-called

house diseases. It is notorious, as the old Germans used to point out, that where the sun does not enter the house the doctor surely will. They appreciate the importance of sanitary homes for good health, and have pointed out some of the factors that are inimical to health, particularly dampness and darkness and gloomy houses, all favoring the predisposition to tuberculosis. We can understand very readily why a dark house and a damp house would tend to prolong the life of a tubercular bacillus which in a healthful house would sooner or later be destroyed by nature's agents.

Dr. Solano spoke in Spanish, which was interpreted as follows:

Dr. Solano says that he has been studying tuberculosis for the last 10 years. He first read a thesis which was well received by the Medical Academy of Bogota, in Colombia, where he studied. He went into the matter as thoroughly as possible; he studied all the statistics that he could get hold of and studied the subject from all points of view. He made studies in the Polytechnic Hospital; there was an epidemic of dysentery at the time, and all these patients suffering from dysentery were taken to this hospital. They would get well from the dysentery but would unfailingly take tuberculosis, which showed that there was contagion taking place. There were some cases of tuberculosis there, and these patients weakened from dysentery would quickly take tuberculosis. He says he finds that the tubercular bacilli are extremely weak, but that they always will attack and will cause disease in an organism that is weakened.

He says that tuberculosis is due at present to the present condition of civilization; that is why he thinks it can be combatted if these conditions are modified and proper measures taken against it.

The CHAIRMAN. I may state that our progress in the combat against tuberculosis in the United States since 1880 has been very gratifying indeed. The death rate from the disease has been reduced from about 326 per 100,000 in 1880 to 147.6 in 1913, which means that if the former rate of mortality had been continued the number of deaths from this disease last year would have been 322,000 instead of 143,000. This is equivalent to a saving of 179,000 lives during 1913 from this disease alone.

This is largely due, I think, to improved personal sanitation, and our campaign in the future must undoubtedly continue along those lines, apart from the specific measures which are necessary and essential for the destruction of the germs wherever we encounter them and for the protection of the people. Our chief aim must be to build up the power of resistance of the individual to the disease. The germs are most ubiquitous. The opportunities for contracting the disease are so general that it is a question of a battle between the microbal invader and the tissue itself.

Therefore our combat should begin with infancy and childhood, practically even with the prenatal care of the child, so that it may be endowed by nature with a stronger resisting power. The hygiene and the general care of the child in the home is of the utmost importance. Next to that, the hygiene of the child in the school, its physical development by agency of playgrounds—they are all important.

Naturally, then, the questions of habitation and food are essential. Anything that will tend to develop a strong vigorous nation will naturally be of the greatest benefit in our campaign, not only against tuberculosis, but against numerous other infectious diseases. The question of pure lives, the question of temperance, the question of freedom from vice diseases, are all important. The matter of factory sanitation in after life is of the utmost importance, because we know that the people who are exposed to the dust of factories are 50 per cent more predisposed to tuberculosis than those not so exposed.

So all our efforts hereafter must be along the lines of personal and public hygiene, and I am very glad that our Pan American colleagues apparently emphasize that same line of campaign in their own country.

Personally I wish to thank the representatives from the Latin-American countries for taking a deep interest in one of the very serious and grave but decidedly hopeful problems, because I believe that if all our knowledge is intelligently applied, and faithfully executed the disease will be actually eradicated between the next 15 and 60 years.

Dr. CARTER. I think we should tell Dr. Solano that a condition such as he describes at Bogota would not be possible in the United States; that practically no hospital treating general cases treats cases of tuberculosis; that such cases are always treated either in special hospitals or in general hospitals in wards isolated from the other patients. How much risk there is in mixing them may be a question, but at least that risk is not taken in the United States; open cases of tuberculosis are not treated in wards where other patients are received.

The CHAIRMAN. Dr. Solano's experience was very much our own in years gone by in America. Many years ago patients who recovered from measles or whooping cough or typhoid fever or dysentery, it was found, were peculiarly susceptible to tuberculosis. No doubt many of those cases contracted the infection in their weakened state, possibly by contact with the disease. We know that when people are as much as 3 feet from each other in a hospital the infections play an important rôle in the transmission of the disease. These contact infections were pointed out 10 years ago by Dr. Edsall, of the University of Pennsylvania. He made a strong plea for what he

called medical hygiene in our ward cases, and all these things are being appreciated and are now being avoided.

I will just add one more sentence. It is, of course, quite possible that in many of the cases where these infections develop the weakened system has simply permitted some latent infection to develop. It does not follow always that a recent infection has taken place, but the reduced power of resistance permits the developing of latent infections, infections that may have been contracted years and years before.

Dr. Solano made some further remarks in Spanish, which were translated as follows:

Dr. Solano says that he has studied different kinds of tuberculosis, especially in Panama among the poorer classes of the people. The suburban towns are populated almost altogether by these poorer people. These houses where they live seem to be infected with tuberculosis. He says he has often observed many obvious cases of gastroenteritis to become tubercular on subsidence of the antecedent attack of gastroenteritis.

The CHAIRMAN. If there is no further discussion the meeting will stand adjourned. All resolutions will go to the committee on resolutions as a matter of course. If there is no further business the session will adjourn.

Adjournment.

JOINT SESSION OF SUBSECTION E OF SECTION VIII AND THE AMERICAN ASSOCIATION FOR CANCER RESEARCH.

NEW EBBITT HOTEL,
Thursday morning, January 6, 1916.

Chairman, LEO LOEB.

The session was called to order at 9 o'clock by the chairman of the section.

Papers presented:

Cancer Problems in Special Biological Groups—

Plant tumors—Further evidence that crown gall of plants is cancer, by Erwin F. Smith.

Fish tumors—Further observations on so-called carcinoma of the thyroid, by Harvey R. Gaylord.

Tissue cultures in cancer. Papers by Robert A. Lambert and Montrose T. Burrows.

A mechanistic theory of cancer, by G. H. A. Clowes.

Radium in experimental cancer, by Francis Carter Wood.

Radium in the treatment of cancer, by William Duane.

Pathological aspects of some problems of experimental cancer research, by James Ewing.

Sero-diagnostic methods in cancer—Reactions of Freund and of v. Dungern, by A. F. Coca.

Teratoma de la región del tuber cinereum, by Guillermo A. Bosco.

The CHAIRMAN. The first paper is on "Plant tumors," by Dr. E. F. Smith.

FURTHER EVIDENCE THAT CROWN GALL OF PLANTS IS CANCER.

By ERWIN F. SMITH,
Laboratory of Plant Pathology, United States Department of Agriculture.

Tumors without visible cause are the subject of this address. They have been studied most numerously in man, but they occur also in the domestic animals, in wild animals (mammals, birds, batrachians, fish) and now, as we know, in plants. If this paper were given a full descriptive title it would read as follows: Further evidence that crown gall is cancer, and that cancer in plants because of its variable form and its bacterial origin offers strong presumptive evidence both of the parasitic origin and of the essential unity of the various forms of cancer occurring in man and animals. This is the text I shall talk to, and in passing I may add it is a view entirely opposed to the current views of cancer specialists.

To make plain what I have to say about plant tumors of this type it will be necessary briefly to mention similar animal tumors. This I shall do without special refer-

ence to medicine, i. e., simply from the standpoint of a biologist, but first I shall show you the gross appearance of a few animal cancers.

These tumors without visible cause are very common in man. They have been observed in every organ and in every tissue of every organ. They have been studied diligently by human pathologists, and especially by morphologists, for many years and there is now a great volume of literature respecting their structure and course of development, but very little is known as to their cause,[1] and nothing as to the occurrence in them of any causal organism.

Clinically and morphologically they are divided into two well-marked groups—the benign tumors and the malignant tumors. All of these tumors, whether benign or malignant, are abnormal overgrowths (cellular proliferations) of the normal tissues of the body. Every organ and every tissue in which a benign tumor has been observed may also become the seat of a malignant tumor. Moreover, benign tumors sometimes behave like or become converted into malignant tumors. Often, in early stages of growth, it can not be foretold whether a given tumor will continue benign or become malignant. Benign tumors are, therefore, always to be considered as a possible source of danger, and their interrelations, if any, with cancers can not be known until their causes are known.

As a rule, benign tumors grow slowly, although often eventually they reach a very large size, exceptionally weighing more than the rest of the body. The cells composing them approximate in form, and in size (that is, in maturity), the cells of the normal tissues. Owing apparently to their slow growth, there is also a body reaction in the form of an enveloping capsule, which shuts off the tumor from the surrounding tissues. These tumors are called "benign" because while they often cause great inconvenience and sometimes death, they are restricted, usually, to the locality where they first appear. That is, they do not develop destructive daughter tumors in other parts of the body.

On the contrary, the cancers, or malignant tumors, with a few exceptions, produce daughter tumors freely (often in vital organs), grow rapidly, are destitute of a restraining capsule—i. e., become invasive, and are composed of cells, which, while showing all grades of transition are often much smaller and more embryonic in their appearance than cells of the tissue from which they have originated, and are then most malignant. These immature cells are readily distinguished, however, from normal embryonic cells both by their disturbed polarity and by their reaction to stains. In other words, they are not genuine embryonic tissue, because they do not possess either the full structure or the entire capability of embryonic tissue. These cance cells proliferate freely, sometimes with astonishing rapidity, invade and destroy normal tissues, and in various ways act like a foreign organism, that is, they behave in the manner of a parasite, although they are a part of the body.

Without including all of the forms known, or going into a swamping multiplicity of details, I may say that the cancers, or malignant tumors, may be subdivided into four principal groups: (1) The sarcomas, which are malignant fleshy proliferations of the various types of connective tissue; (2) the cancers proper, or carcinomas (including the epitheliomas) which are destructive (eroding) proliferations of the epithelium of the skin, mucous membrane, and glandular tissues generally; (3) the so-called mixed tumors containing proliferating elements from two germ layers, e. g., the chondro-sarcomas composed of proliferating cartilage and connective tissue, the adeno-sarcomas composed of glandular tissue and connective tissue, etc.; and, (4) the embryonal teratomas which, in addition to the cancerous element that is often a sarcoma, contain teratoid elements representing all three germ layers—young tissues of various organs,

[1] Dass das Dunkel auf diesem Gebiete noch nicht erhellt, des Rätsels Lösung noch nicht gefunden, das zeigt die noch stetig zunehmende Fehde der Streiter auf diesem Felde. Hie embryonaler Keim, hie parasitärer Ursprung, hie Metaplasie, hie Anaplasie, hie Anarchie, so lauten die Schlagworte der Autoren Wilms).

frequently an astonishing mixture of teratoid elements, but all embryonic. These are also known as atypical teratoids in distinction from monsters, which are prenatal malformations, and from typical (ripe or adult) teratoids which also are not cancers, but growths due to prenatal disturbances, the commonest form of which is the ovarian dermoid. By Wilms they are called solid embryomas or embryoid tumors in distinction from the typical teratoids, which he calls cystic embryomas or simply embryomas.

The atypical teratoids grow rapidly, metastasize freely and are commonest in the early decades of life. In the typical teratoids the fetal fragments have grown with the growth of the host. Although dwarfed, they are as old as the individual out of which they have come, i. e., they contain old skin, old teeth, old bones, long hair, etc. In the atypical teratoids the fetal fragments are always very embryonic and probably are never more than a few months old, or a few years old, no matter how old the person from whom they have been removed, i. e., growth goes on in them independently of the host. Moreover, these atypical teratoids always contain cancerous elements. It is this latter type of tumor that I have recently produced in plants.

In the benign tumors, to return to animals, the tissues are arranged in a nearly or quite normal fashion and the cells are full grown, only much more abundant than they should be. In the malignant tumors the tissues are not only more embryonic, but are arranged atypically, the cells having lost a part or the whole of their polarity, i. e., their orderly arrangement. Frequently they also show defective mitosis, and very frequently polynuclear cells (the so-called "giant cells") appear, owing to fission and fragmentation of the nucleus without any corresponding cell division. Lobed and cleft nuclei are very common in cancers. They are also common in crown gall.

Cancers in addition to the malignant cells contain a stroma or framework of connective tissue and a system of blood vessels and lymph channels by means of which they are nourished, but the blood flow in these vessels is not controlled by any vasomotor nervous system. Ordinarily cancers do not contain any nerves, the associated pain being due to pressure on outside nerves.

All of these tumors are imperfectly provided with blood vessels and are subject to early decay, the resulting cavities, or open wounds, being exposed to various harmful secondary infections. In early stages of growth these tumors are purely local and may be removed surgically with good prospect that they will not return. In late stages these tumors exert a markedly detrimental effect on the whole body, which is visible as atrophy, anemia, and cancerous cachexia, and surgical interference is then of little or no avail.

The daughter tumors are produced from the mother tumor in several ways, i. e., by contact of a diseased area with a healthy area, as for example, by tongue against lips, or cheek against jaw; by invasive growth, i. e., tumor strands out of which the secondary tumors develop as in cancer of the breast; by motile (creeping) tumor cells; or finally, by cells or fragments dislodged by the blood stream or the lymph stream and carried to distant parts, where they multiply. The carcinomas usually invade by way of the lymphatics; the sarcomas and the embryomas, by way of the blood vessels. When a tumor strand can be traced from the daughter tumors back to the mother tumor they are called invasive growths; when no such connecting link is visible they are called metatsatic (or shifting) growths. Some modern writers, however, use the word metastasis for a daughter tumor of any origin.

As I have said, nothing is known respecting the cause of these human tumors and the great majority of cancer workers have come to the conclusion (which I believe is erroneous) that they can not be due to parasites.

It is well here to pass in review some of the objections to a parasitic theory of cancer: (1) Because many authors of distinguished reputation (Ribbert, for example) maintain that they are insuperable; (2) because so long as they are not met various persons

will be discouraged from undertaking active researches designed to uncover the parasite; and (3) because, finally, if I can convince you that crown gall is a cancer, you will then be ready to admit that what requires a schizomycete for its production in the plant is not likely to be produced in any very different way in man and animals. Here then are some of the objections, and I will meet them as fairly as I can.

1. Nothing definite in the way of a parasite has been made out by use of the microscope. Answer: This is admitted, but it proves nothing. If we exclude the Negri bodies, still in dispute, the same is true for rabies. And in cancer we have the Plimmer bodies and other cell inclusions of a doubtful nature, some of which may be bacterial or protozoan. The etiology of crown gall would still be in doubt if we had depended solely on the microscope, for no ordinary staining will demonstrate a bacterium in the cells, and yet it is there. For the final analysis recourse must be had to cultures and inoculations. There are then some problems in pathology which never can be solved simply by the use of the microscope.

2. From cancer no parasite has been isolated in spite of diligent bacteriological search. Innumerable cultures have been made and many inoculations and all have failed. Answer: The same is true of yellow fever. No parasite has been found. Until recently the same was true of syphilis. Ten years ago it was true of crown gall. There may be some very special reason (as in crown gall, or in certain types of arthritis) why isolations have failed; or the right organism may have been isolated and inoculations may have failed simply because the inoculated animals were normal, i. e., fully protected by their leucocytes and therfore not susceptible. We must, I think, conceive of cancer as developing only in a weakened, unprotected condition of the body. The more or less ready growth of grafted cancer in certain animals offers no real contradiction because here the conditions are somewhat different from what they would be in case of a naked bacterial inoculation, because the grafted cancer cells are autochthonous cells and are introduced into the mouse or other experimental animal in a considerable compact mass, the inner cells shielded by the outer ones and all developing a kind of protective aura under the influence of which union with the host tissues takes place and the cancerous growth continues.

3. Heredity is a sufficient explanation. Answer: The same thing was said repeatedly of tuberculosis prior to 1884. Now we see that heredity furnished the canvas but could not paint the picture. Miss Maude Slye's work on heredity of cancer in mice is astonishing and praiseworthy, but I do not feel sure that a similar picture could not be obtained by breeding together tuberculous animals, indeed I am quite certain that the results of such experiments would be a vastly increased number of tubercular animals, and if we knew no more about the cause of tuberculosis than we do about the cause of cancer, the interpretation of the results would be entirely wrong, i. e., they would be ascribed wholly to heredity, whereas we know that two factors are involved: (1) Heredity, (2) infection. I do not think Miss Slye has established the fact that cancer follows Mendel's law.

4. There is no need to postulate any parasite, since the cancer cell itself is the all-sufficient parasite and no cancers can be produced in the absence of this cell. Answer: It is strange that the authors of this statement, which has been dinned into us for a generation, can not see that it is no answer at all, but only a makeshift. As well say: Tetanus is due to tetanin. Certainly, we all admit this, but what originates the tetanin? and what originates the cancer cell? Moreover, loath as these objectors are to admit it, cancers (sarcomas) in barnyard fowls can now be induced by cancerous material all the cells of which have been removed by filtration, or have been killed by heat, by freezing, or by drying (Rous). And how should anemias and cachexias arise as the simple result of the proliferation of body cells? In other diseases they are the direct result of bacterial or protozoan multiplication in the body. In this connection reflect for a moment on what goes on in streptococcal arthritis, in persistent agues, or in yellow fever and in blackwater fever where the red blood corpuscles are

destroyed wholesale. Even pernicious anemia will, I believe, be traced eventually to a blood-destroying parasite. All that we yet know definitely concerning the natural occurrence of anemias (I am purposely excluding surgical ones) is that in certain diseases they are due to blood-destroying parasites, and it is not going very far afield to assume that anemia is so produced in cancer.

5. The idea of a parasite is too complex. We know that we can graft cancer only within the narrowest limits, and also that within the same species each sort of cancer reproduces its own kind. We must therefore postulate not only as many different cancer parasites as there are animals subject to cancer, and that is probably every kind of animal, but also a parasite for every special kind of cancer in each particular animal which is a reductio ad absurdum. Answer: This is a molehill magnified into a mountain—an unsubstantiated and unwarranted hypothesis! The history of science is full of such objections. Against the plainest evidence it is always easy for certain types of mind to raise objections, which then generally are left to some one else laboriously to test out experimentally, whereupon they vanish into thin air, the objections not having been well grounded. Some people are good only as objectors! They can not do anything concrete. It is less than 20 years since certain theoretical Germans were saying: "There are no bacterial diseases of plants and can not be any, for the reasons we have given." Yet the experimental method has demonstrated the existence of nearly a hundred. In science, no theory is worth a picayune that does not have an experimental basis under it. There have been at least 30 so-called explanations of cancer origin propounded during the last half century, not one of which really explains or has any experimental basis under it. Cohnheim's theory is one of these: Ribbert's is another.

From the behavior of the cells of one species when grafted on another species we can postulate nothing as to what a naked microorganism would do under the same circumstances. As a matter of fact, plants also can not be grafted widely, yet the crown-gall organism is widely inoculable. Moreover, it yields one result when inoculated into one set of tissues and a different result when inoculated into another set of tissues. In malignant neoplasms in man, and the lower animals, why then may we not assume for experimental purposes an intracellular parasite capable of producing sarcoma when infecting connective tissue cells and other types of tumor when infecting other tissues—each tissue presumptively developing according to its own type? Theoretically I can see no objection to this view, and actually we have this very thing occurring in crown gall.

6. Parasites destroy cells. They do not cause them to proliferate, and calling cancer a cell symbiosis does not help matters. Answer: The world progresses and new knowledge modifies or supplants the old. Menetrier, of Paris, without knowing anything about our experimental work on crown gall, and being very sceptical as to the parasitic origin of cancer, saw clearly in 1908 (and so stated in his book) that there was no objection theoretically to assuming that in cancer there might be a parasite which did not destroy cells, but continually stimulated them to divide, only he said: What is the use of speculating, since nobody has shown any concrete example? This may have been true of that time, but it is no longer true, since there is just such a cell parasite, or cell symbiont, in crown gall.

7. In cancer, portions of the body grow in places where they should not, having come to the place by growth-extension from the primary tumor or having been transported there by a blood stream or a lymph stream. Nothing like this occurs in any parasitic disease. Answer: Formerly this statement corresponded to our knowledge but now it does not, because just this thing occurs in the parasitic plant disease of which I am speaking, viz, invasion or growth-extension from a primary tumor resulting in the occurrence of secondary tumors in what previously were normal parts of the plant.

8. Direct stimulation of cell growth by a parasite is an unknown occurrence in biology. In all cases in which parasites are found within cells the effect is the destruction either of the parasite or of the cell. Answer: Antiquated information. True of many things but not of all. Theoretically a third possibility exists, and actually we have it in crown gall. Here the parasitized cells are not destroyed, neither are all of the bacteria within them killed, but only most of them. There is a very delicate balance between the two, which results not in death of the host cells, but in an increased tendency to cell-division, a tendency strong enough to overcome the physiological control of the plant. When death results it is not due to the direct action of the bacteria, but to other factors, e. g., nutritional defects, and secondary parasitisms.

9. Since cell proliferation in tumors is similar to cell proliferation under normal conditions, the assumption of a parasite to explain it is quite unnecessary, and makes an explanation of tumor-growth more difficult. Answer: Similar is not necessarily the same. Conclusions drawn from cultures in vitro do not necessarily apply to growth within the body. Cell proliferation of tumor tissues in the body is similar, of course, to normal cell proliferation, but with a difference, namely, in the tumor there is an unknown something, which compels these cells to proliferate in opposition to the needs of the body and in spite of the physiological body control. Surely something very foreign to the body is required to explain the undifferentiation, anaplasia we call it, following von Hansemann, and the excessive vegetative force of the cancer cells. Moreover, so far as it is able to do so, the body treats individual cancer cells, or groups of cancer cells (metastatic fragments) exactly like parasites, that is, it envelops them in a blood clot and destroys them. In cancer, therefore, considering what takes place in crown gall, I think we are warranted in searching for an intracellular parasite, probably some common organism, as the unknown factor, necessary to satisfy the equation and explain the phenomena. Moreover, I fail to see how the assumption of a parasite makes the explanation of tumor growth "more difficult." These objectors are here dealing with one of their many assumptions while I am dealing with a fact. I insert my infected needle and I obtain a tumor. I insert a sterile needle and the wound heals normally. Into one branch of a young Paris daisy I set my infected needle 50 times and obtained 50 tumors; at the same time into the twin branch I set a sterile needle 50 times and obtained no tumors whatsoever, but only a normal healing of the wounds. Cell proliferation per se in no way explains cancer. Normal cells, also, judging from the way they behave in blood serum under the microscope, must often proliferate into the plasma of the body, but such wandering cells are promptly disposed of in accordance with the law of antagonism or of physiological control, or whatever you please to call it. I mean the action of the body as a whole. Otherwise, we should have occurring continually in the body what takes place when normal tissues are cultivated in vitro, that is, a copious cell proliferation, which would be disastrous. This we do have in cancer, but since cancer develops in opposition to all the compelling forces of the animal body it must be owing to a profound disturbance of the normal (interior) activities of the cells involved. What is so likely as a microorganism to produce this cell disturbance leading to the formation of a tumor? Especially what, since in the plant we know that one does produce just that?

10. Cancers are due to long-continued inflammatory conditions. They begin in bruises, in old (unhealed) wounds, X-ray burns, charcoal stove burns (Kangri cancer), and various irritations and injuries incident to special trades (chimney sweeps' cancer, paraffin workers' cancer, etc.). Answer: The second statement is admitted. They begin in all of these places. The first statement is a non sequitur, a post hoc ergo propter hoc argument. Wounds are often infected with visible parasites, why not sometimes with invisible ones? Not all irritations end in cancers. Of two long-continued irritations one may become malignant and the other not. This is wholly inexplicable on the theory of simple irritation, but readily interpreted if we assume that cancer is due to a special and unusual kind of parasite, certain long-continued

irritations having paved the way for a peculiar infection by having reduced the resistance of the body.

11. Surgeons, nurses, and relatives do not contract cancer. It therefore does not behave like a communicable disease. Answer: Neither does malarial fever; neither does arthritis; neither does leprosy; and, finally, neither does crown gall. We must recognize that in nature there are all grades of parasitism and must be prepared to welcome forms not hitherto recognized. In pathology, as everywhere else, the open mind is after all the best asset. Closed and crystallized minds are of no further use in the world. Certainly cancer is not an acute infection, and no one regards it as such. It may be due, however, to a parasite, visible or invisible as the case may be, some feeble parasite against which the normal body is fully protected, some common organism, living saprophytically on the body, or in the soil, able only to infect a depleted body, and destructive only when through wounds (very slight ones, it may be) it has penetrated into the interior of certain cells, which neither kill it nor are killed by it, but where it depresses functional activity while at the same time enormously stimulating vegetative activity. In the present state of our knowledge no one can say that this is an untenable working hypothesis. Indeed the probabilities in favor of such a view are much stronger to-day than they were five years ago, when I first discovered the cancerous nature of crown gall and began to formulate my ideas.

12. We might, possibly, concede sarcomas to be due to a parasite, but not carcinomas, and certainly not embryomas, yet whoever proposes a parasitic theory of cancer must not only demonstrate his parasite but with it must account for all of these diverse forms, and especially for embryomas, since they are the crux of the whole situation.[1] Answer: This is admitted. All of these forms hang together, and the claim is now made that embryonal teratomas and gland proliferations can be induced with the same schizomycete previously used to produce sarcomas. As a negation it is of no consequence whatever to say that I have only produced them in plants, because, little as it is yet recognized, plants are better adapted than animals to certain purposes of cancer research. In due time and in the same way, let no one doubt, they will also be produced in animals. Whatever else may be denied, the bold fact now stands out demonstrably that all the leading types of cancerous proliferation can be produced in plants with one microorganism. If anyone doubts it, let him repeat my experiments.

13. But this hypothesis of the origin of cancers, and especially of embryonal teratomas upsets Cohnheim's theory of "cell rests." Answer: It does, beyond doubt, very completely. But there is no use of making a fetish of Cohnheim's theory. It is, after all, only a theory. It seemed once to furnish the basis for an explanation of cancer origin, but no one was ever able to build a superstructure on it, for no one can explain why some "cell rests" grow into cancers while others, and by far the larger number, remain dormant. We shall simply have to write Hic jacet over Cohnheim's theory. It serves well enough for monsters and for typical teratoids, but it does not explain cancers.

14. Plants are so unlike animals that no comparison can be drawn from diseases of the one group to those of the other group. Answer: On the contrary, fundamentally plants and animals are very much alike. I mean the resemblances are much more basic than the differences. The latter, very conspicuous to the eye, may be regarded as differences of degree rather than of kind, corresponding to differences in function. Such an objection could never be raised by a biologist. It shows perhaps better than any other argument how great is the need of injecting biological concepts into cancer research. The cancer problem would have been settled long ago, I believe, had it

[1] Gerade in diesem Punkt scheint mir die interessanteste und wichtigste Beziehung der Teratomen zu den anderen Geschwülsten zu liegen, dass wir in den Teratomen eine Gruppe von Produkten vor uns haben, in welcher sich die Hauptfragen der Geschwulstlehre wie in einen Brennpunkt vereinigen (Borst).

been approached commonly from this angle rather than from that of pure morphology. Of many of the lower forms of life it is still very difficult to say whether they are plants or animals, of the whole group of bacteria, for example; and for the primitive, doubtful forms of life you will recall that Haeckel created the special kingdom of Protista. To my mind a fundamental unity runs through all living things from the lowest to the highest, like the gold thread through a tapestry. For one thing, all are alive; all possessed of that unstable equilibrium of forces expressed by the words growth and decay. These phenomena are the properties of a substance called protoplasm. In both plants and animals this substance is organized into the form of cells. In both, usually, it is the outer protoplasmic membrane that controls the passage of ions, the disassociated electrically charged elements of water and other compounds. The same wonderful process of cell multiplication by mitosis occurs in both plants and animals. In both, except in the lowest forms, these cells are organized into tissues with division of labor. In both there is a sexual method of reproduction. Plants, indeed, propagate also nonsexually by budding, but so do many of the lower animals. In many plants there is regeneration when parts are cut away, but so there is in a great variety of animals. Even their foods are not different. It is true the plant differs decidedly from the animal in possessing an apparatus for elaborating inorganic substances into starch, sugar, and proteids which the animal consumes, but it makes these substances for its own use, not for the animal. It is sometimes assumed that the inorganic substances of earth, air, and water are the food of the plant, but such is not the case. The plant depends for its growth on the same nutrient substances as the herbivorous animals, viz., on starch, sugar, and proteids, which it has stored in every seed and under every growing bud. The phenomena of birth, growth, and decay are essentially the same in plants and in animals; but corresponding to higher development the animal has many special organs either wanting altogether in the plant or greatly simplified; it also has flexible cell walls while the plant has rigid cell walls; but both plants and animals respire; both assimilate food substances and oxidize them with resultant work; both require about the same amount of water and mineral salts; both have a circulation of fluids; and both secrete and excrete a variety of substances, acid, alkaline, and neutral. The response to stimuli, such as gravity, heat, light, radium, X-ray, electricity, and poisons, is much the same in both groups. In irritable response plants and animals both obey Weber's law (called also Fechner's law and the psycho-physic law), that is, to increase a response in an arithmetical ratio the stimulus must be applied in a geometrical ratio. There is a suggestion even of a nervous system in plants since stimuli are passed along certain channels to distant organs and the movement can be slowed down by cold, increased by heat, or inhibited by poisons applied midway, the response, according to Bose, being not simply hydromechanical. Even the idea of locomotion does not distinguish animals from plants. Many of the lower animals are rooted fast, while many of the lower plants have swimming organs and are actively motile. Moreover, all of the higher plants change position more or less; all are sensitive; all show rhythmic movements. Finally, the intimate cell chemistry of the two groups (production of digestive enzymes, amino acids, etc.), so far as known, is much alike. There is no a priori reason, therefore, why a special stimulus to cell division in plants might not prove to be of the highest interest to students of cancer in man and the lower animals. It is a matter to be taken up like any other and tested out; Researches on crown gall should have been undertaken long ago in every cancer laboratory in the world and would have been had we not unfortunately discovered a parasite. That killed the whole subject in the eyes of the orthodox. Not having found a parasite themselves, they will not believe that anyone else can do it or that there is one; and this in spite of the fact that the history of parasitic diseases from Pasteur's time down shows clearly enough that the folly of one generation has been the wisdom of the next.

Von Hansemann has said [1] that crown gall has nothing in common with cancer except its name (Krebs). I am quite willing to let specialists weigh my evidence and decide for themselves, if only they will wake up and begin to do so; not simply ignore the whole subject because it comes to them from an unusual quarter and is "too botanical," as another German editor said in refusing one of my papers.

In his "Principles of pathology" [2] Dr. Adami gives the following as the characteristics of the atypical (malignant) tumors: (1) Vegetative (embryonic) character of the tumor cells; (2) rapidity of growth; (3) peripheral extension, lack of capsule and infiltration of the surrounding tissues; (4) tendency to develop metastases; (5) tendency to central degenerative changes; (6) liability to recurrence after removal; (7) cachexia; (8) anemia. All of these occur in crown gall except (4) and (8). There is nothing in the plant corresponding to blood, and the rigid cell-wall of the plant prevents metastasis in the true sense of that word. But if we use the word metastasis in Ribbert's loose way, then metastasis also occurs in crown gall.

One of the striking things about cancer and one separating it off sharply from all other animal diseases, is the fact that the secondary tumors are not granulomatous proliferations. That is, the secondary tumors are not a growth response of local tissues to an irritation, and hence are not comparable to the protective granulations formed in the healing of a wound or in such a disease as tuberculosis, but they are due to the migration from the initial tumor either of infected cells or of deteriorated cells which continually reproduce their own kind to the detriment of all others. The cancer cell is a lawless entity, different in its tendencies and capabilities from any other cell of the body, and so far as we know, it always reproduces its kind, the daughter cells being cancer cells and not normal cells. Why this is so is wholly unknown in human and animal pathology, but that it is so admits of no doubt whatever. To illustrate: If medical men were able to reach into the center of tubercle nodules or syphilitic nodules in the human body, and kill the nest of pathogenic bacteria in the one case and of pathogenic protozoa in the other case, without injuring the unparasitized barrier cells forming the periphery of these nodules, then these cells would be immediately destroyed and removed from the body as no longer of use, or else would behave once more as normal body cells (scar tissue). In cancer, on the contrary, as every surgeon knows, if any cancer cells are left after an operation—even the least number—they are likely to reproduce their evil kind, in which case another tumor results either in the old locality or in some other part of the body. In other words, the outermost cancer cells are not barricades erected by the body to prevent further encroachments of the enemy, but are self-multiplying outposts of the enemy himself. However, this does not militate against the belief that some of the elements in a malignant tumor are harmless ones, nor that the body often reacts against the tumor as a whole by the formation of fibrous tissue, and in other ways.

Very few laymen, I believe, have any clear conception of the exact mechanism of the cancerous process, and not a few physicians also seem to be ignorant of it. Cancers are the result of the multiplication in the body of certain body cells which have become abnormal and dangerous to the rest of the body, or as we say "cancerous," a single cell or a few cells to begin with, then many. Whether infected or only degenerate, these cells retain their hereditary tendencies, that is, liver cells to reproduce liver; brain cells, brain; connective tissue cells, connective tissue; and so on; but all of them while deriving nourishment from the body have become more or less emancipated from body control and exercise their freedom by an unlimited and hasty multiplication very destructive to the other tissues of the body. They reproduce their kind first in the primary tumor and later in secondary tumors. I can make this plainer perhaps by another illustration. Following tuberculosis of the lungs there sometimes occurs blood infection and a generalized tuberculosis of every organ in the body, but in such cases the nodules wherever they arise are due to local bacterial

[1] Zeitschrift für Krebsforschung, 12te Bd., 1913, p. 146.

[2] Vol. I., p. 671.

irritation, and are always built up out of local tissues, liver tissue in the liver, spleen tissue in the spleen, and so on. In cancer, on the contrary, it is the cancer cell which migrates with all its hereditary tendencies and the secondary tumor, therefore, reproduces more or less perfectly (or imperfectly) the hereditary cell complex of the primary tumor, so that the trained pathologist after studying sections of a cancer can usually (but not always) decide whether it is primary in the organ under examination, or secondary; and if secondary, then in what other organ the primary tumor is to be sought. For example, if a primary cancer occurs in the liver and there are metastases to the lungs the lung tumors will contain liver cells; so if a primary cancer occurs in the stomach and there is metastasis to the liver, the liver tumor will not be formed out of liver cells but out of stomach cells. It is a very striking thing to see under the microscope, particularly in a well-stained section, a nest of malignant glandular stomach cells in the midst of a piece of liver. I do not know that it has been actually proved, but undoubtedly such a liver tumor must have the power of secreting pepsin or at least of mucin, just as we know that metastases from a primary liver tumor into other organs may retain the power of secreting bile.

I have now come to another way in which these plant tumors resemble cancer in man and the lower animals, viz, in the striking fact that as in animals the secondary tumors reproduce the structure of the primary tumor. Thus when a primary tumor is induced on a daisy stem by inoculation, deep-seated secondary tumors, developed from parenchymatic tumor-strands, often arise in the leaves, and these tumors convert the unilateral leaf or some portion of it into the concentric closed structure of a stem. (Slides shown.)

Having now reviewed my older discoveries,[1] I come to details of more recent ones also bearing directly, I believe, on the etiology of cancer.

I have referred to the rapid growth and early decay of cancers in men and to the common occurrence of atrophy and cachexia in connection with such tumors. Similar phenomena occur in the plant. I show you three slides from photographs of galled sugar beets. They were grown in different years (1907, 1913, and 1916), but each showed the same thing, viz, sound control plants and dwarfed, sickly (yellow), and dying inoculated plants. Each inoculated plant bore a tumor larger than itself, and the time from inoculation to date of the photograph varied from 2½ to 4½ months. This year I have obtained the same results on ornamental (white flowered) tobacco. At the end of five months all of these inoculated tobaccos are dead or dying from large tumors of the crown, whereas the control plants are healthy, many times larger, and now in blossom. To get such prompt, disastrous results, the inoculation must be fairly early in the life of the plant and near the growing point.

Secondary infections due to other organisms are also as common and as disastrous in crown gall as in cancer in man. Just now in the hothouses we have striking examples of it on the Paris daisy, and I will show you a few slides. (Slides.) These secondary infections may be either fungous or bacterial.

Third, let me show you some examples of infiltration, taken from sunflower heads inoculated last year. The first three slides show hard greenish-gray vascular tumors which have developed from a few needle pricks made into the extremely vascular thin layer which bears the seeds. The one shown in vertical section is from the middle of the flower disk, and it has grown downward in the white pith for a distance of 4 inches. It lies in the pith but has not developed out of pith. The fourth slide from another tumor shows cancerous cells and vessels of the supporting stroma pushing out into the sound tissues much as roots do into a fertile soil. The fifth slide is from the cortical part of a teratoma on Pelargonium. Here the small-celled blastomous tissue has crowded in between coarse cells of the cortex.

[1] See Science N. S., Vol. xxxv, p. 161.

Next to be considered are examples of atypical blastomous tissue taken from different parts of the same tumor (a young deep inoculation into the stem of a Paris daisy). In the first slide, at the left, is a part of the supporting stroma (cortex cells); the right side shows round cells of the same type that have become cancerous, i. e., much smaller, more embryonic, rapidly proliferating, large nucleate and deep-staining cells which have lost their polarity. The second slide shows spindle-shaped blastomous cells from the outer part of the same tumor. This tumor is the ordinary rough gall of the daisy stem, which is a sarcoma as near the plant can make one, that is, a sarcoma minus the intercellular fibrils which are wanting in plants.

Now let us consider how plastic the living tissues can be when they are brought under a cancer stimulus. I show you photomicrographs of tumors (atypical hyperplasias) produced by inoculating the crown-gall organism into the extreme outer bark (living cortex) of young stems of Paris daisy, the inoculated cells being ordinary cortex cells. These tumor cells which conceal the bacteria (there are none in the intercellular spaces) have become more embryonic than the tissue out of which they have grown. This is shown by their size (one-twentieth that of the cells from which they have developed), their large nuclei, and their avidity for stains, as well as by the peculiar way in which they fix the stains. It is also shown by the fact that they can produce vessels in their midst (tracheæ), whereas the uninjured cortex never produces vessels. The embryonic tissues of the plant, however, have this vessel-producing power. In a word, these tumor cells have become more embryonic than the tissue out of which they have developed and have lost their polarity, and this is exactly what occurs in cancer in man, as I shall show you. I have produced these superficial fine-celled hyperplasias out of coarse-celled cortex, not once but a number of times, and in several different kinds of plants.

Thus far I have spoken only of one type of tumor, the common crown gall. Until this winter (if we except hairy root) I did not know of the existence of other types. Now I believe from what I have seen that all the leading types of cancer, viz, (1) sarcoma, (2) carcinoma, (3) mixed tumors, and (4) embryomas, occur in plants, and that all are due to one and the same organism. I certainly have abundant material of the end terms (Nos. 1 and 4), and enough of 2 and 3 to convince myself, if not others.

The "further evidence" alluded to in the title of this paper relates more especially to the embryomas and consists of the discovery of an entirely new type of plant tumor due to the crown-gall organism, in which tumor there are not only ordinary cancerous cells of the common crown-gall type, but also entire young shoots or jumbled and fused fragments of leafy shoots and of other young organs, thus making the tumor correspond to the highest type of animal cancer, in which in addition to the blastomous element there are fragments of various fetal tissues, sometimes representing many organs of the body. This is, I believe, the first time this type of tumor has been produced experimentally, and it has been done with the bacterial organism cultured from an ordinary rough crown gall of the simpler, well-known type. It was first done by inoculating the leaf axils of growing plants, i. e., the vicinity of dormant buds, in other words, centers containing totipotent cells. Some of these strange tumors have produced daughter tumors in other parts of the stem and in leaves and, as in the embryonal teratomata in man, a portion of these secondary tumors have the full structure of the primary tumor.

I have also produced these teratoid tumors in parts of plants where no totipotent cells are known to exist, but only young plastic cells normal to the parts and hitherto supposed to be able to produce only one kind of organ. This will be plainer if I say that by needle pricks introducing the bacteria locally I can now produce atypical teratoid tumors in internodes and in the middle of leaves, an astonishing discovery, and one bound, I believe, to revolutionize our views as to the origin of these tumors in man. I do not here deny that totipotent cells, hitherto unsuspected, occur in the places I have inoculated; indeed they must so occur, but I only cast doubt on their abnormal occurrence in such places, i. e., as the result of early embryonic dislocations.

The belief that I have also produced "mixed tumors," that is, tumors containing distinct types of tumor cells originating from different layers of the plant, rests on stained sections of tumors from several different kinds of plants. The evidence here is not as complete as in the case of the embryonal teratoma, and I am still experimenting. What I think I have in one part of the tumor is sarcoma originating from the deeper connective tissue layers and in another part of the tumor carcinoma derived from the skin and glands of the plant. However this may be, it is now beyond question that two very distinct types of plant tumor (sarcoma and embryonal teratoma) corresponding to similar types is man, as nearly as plant tissues are able, can now be produced by bacterial inoculations, using the same organism. To get one type of tumor I inoculate one set of tissues, and to get the other type, another set of tissues.

Coming to the details of my newer studies, I shall first take up the question of the possible existence of carcinoma in plants, the slides I shall show you being from photomicrographs of what I consider to be "mixed tumors." All are due to pure-culture inoculations, but they show a diverse internal structure suggestive of a mixture of epithelioma (skin cancer) and sarcoma (connective tissue cancer). There is still, perhaps, some doubt as to the interpretation of these facts, so that I speak only with reserve and subject to revisions due to further experimentation.

The first slide I show you is from a teratoma on the common Pelargonium or house geranium, but in this connection I invite your attention only to a small portion of its surface (teratoid part) where strange phenomena are in progress, quite like what often occurs in the epithelium of human teratoids. Here is a compact, small, surface tumor showing subepidermal erosion, an effort on the part of the plant to protect itself. Its deeper tissues fuse into those of the epidermis in such a way as to suggest that they have originated from the latter—i. e., there are no epidermal and subepidermal differences, although these differences are conspicuous in the normal plant and also in other parts of the teratoma. In this late stage of development it is impossible to tell what may have been the origin of these queer tumors, but what appear to be much earlier stages of the tumor are visible in several places, especially on their margins, and these places exhibit, or seem to exhibit, all stages of transition between the normal one-layered faint-staining columnar epidermis (equivalent to an epithelium), and a several-layered, large nucleate, loosely arranged, deep-staining tissue, the cells of which are rounded or angular and have lost their polarity; that is, their orderly relation to their fellows. Now, this is exactly what takes place in early stages of carcinoma. For instance, below the one-layered epithelium in glandular tissues of breast, of stomach, etc., irregularly placed, large-nucleate, deep-staining, rapidly proliferating cells make their appearance as shown on the next slide, which is from a cancer of the lung. This kind of proliferation is recognized as the beginning of a malignant tumor, and surgeons base their operations on its presence or absence. If, in the breast, let us say, this displacement of cells is present, then the surgeon does a major operation, but if it is not present, then he is content with having removed only the local nodule. These surface tumors on the geranium were accidental discoveries, but I have now begun a systematic inoculation of the skins of plants to see what I can get.

I have what I believe to be the same phenomenon (a mixed tumor) on tobacco. This tumor I produced out of young cortex in 1907, but it has been properly stained and critically studied only recently. Its outer part consists of blastomous cells quite different in shape and staining capacity from the cells of its inner part. The outer cells are more or less compact and angular and the protoplasmic contents stains uniformly. The inner cells are round, more loosely arranged, and stain like the ordinary sarcoma cells of this tumor. In connection with the last slide I would also call special attention to the evidence it shows of the appositional transformation of normal cells into cancer cells (atypical blastomous cells). I refer to the band of

tissue lying between the normal cortex on the right (out of which the tumor has developed), and the fine-celled hyperplasia on the left. These 10 or 12 rows of cells, bordering the tumor, have the same arrangement as the tumor cells and stain deeply like those of the tumor, but are several times as large. Occasionally an unchanged cortex cell is buried in their midst. They are, I believe, a transition from the normal tissue into cancerous tissue.[1] The same phenomenon has been seen in human cancers by several good observers and there can be no doubt as to its occurrence.

Finally, from shallow bacterial inoculations done on the glands of Ricinus last winter I have also obtained what appears to me to be satisfactory evidence of glandular proliferations—i. e., rapid multiplication of the surface layer of cells with loss of form and polarity and entrance into the subepidermal region as an invasive hyperplasia. The punctures were deep enough, however, to have infected the subglandular connective tissue which is also proliferating. The sections were cut at the end of 27 days and show transitions from a columnar (glandular) epidermis into an irregular, angular-celled, large-nucleate, deep-staining mass of rapidly multiplying atypical cells corresponding to an epithelioma (slides). The shape of these cells is exactly that of proliferating epidermal cells from my one-one hundredth millimeter deep 72-hour inoculations on tobacco stems. I have not yet obtained metastases from such surface growths, but I am only now beginning my studies of skin and gland proliferation and there is much to learn.

We now come to embryomas. Before describing the atypical teratoid tumors I wish to make some general remarks. Conceiving human and animal cancer to be due to a parasite, I have been greatly interested for the past 10 years to see to what extent the phenomena of such cancers, the cause of which is unknown, can be paralleled by crown-gall phenomena the cause of which is an intracellular schizomycete. By discovery of a tumor strand and of stem structure in leaf tumors (in 1911) my interest received a tremendous accession from which it had not yet recovered when the newer discoveries of this winter converted it into a white heat. I am now persuaded that the solution of the whole cancer problem lies in a study of these plant tumors. At least they must now be studied until the matter is definitely settled, pro or con.

If cancer is due to a microorganism, bacterial or other, we are not obliged theoretically to conceive of all such new growths as due to one and the same parasite, nor, indeed, on first thought, is such the more probable hypothesis. The first thought is that probably there must be as many parasites as there are kinds of tumors, yet certainly, on further reflection, the mere cell differences between a sarcoma, let us say, and a carcinoma do not necessarily involve the conception of two parasites. The two tumors can be explained theoretically just as well by the postulate of one parasite, and in the light of our researches on crown gall much better by one. If the tissue response depends on the kind of cell or cells first infected, as apparently it must, on the assumption of a parasitic origin, then, of course, if connective tissue cells only are involved, we shall have sarcoma; if gland cells only are invaded we shall have carcinoma; or, if both, then a tumor containing both types of cancer. Whichever cell was first invaded (the bacteria being imprisoned) would be likely to continue its proliferation as a tumor of a pure type, but other elements might eventually become infected by a surgical operation, or otherwise—e. g., a sarcoma might follow a carcinoma as in some mouse tumors, and also in man, the connective tissue stroma becoming infected.

I now think the human embryonal teratomata are cancerous not only potentially but actually from the beginning. Many of them have been recognized to be so on removal, and in the remainder the stimulating blastomous portion may have remained undiscovered owing to its relatively small size, as was the case in hairy root of the apple (and every particle of such a tumor would have to be sectioned and

[1] See the Journal of Cancer Research, April, 1916, Pl. xxiii, fig. 78.

studied before one could deny it), or it may have receded during the rapid development of the nonblastomous purely teratoid portions. All of them, whether it be assumed that they have developed from "cell rests" or parthenogenetically, are, I believe, due to the stimulus of a microorganism, but not necessarily of a schizomycete, since other orders of parasites may, conceivably, give rise to the same chemical and physical stimulus.[1]

Wilms in his book on "Die Mischgeschwülste" (Heft 3, Leipzig, 1902, p. 242), if I understand him correctly, considers the blastomous portions of embryoid tumors to be of a secondary nature, as do other writers, but in this assumption they are probably wrong.

To the statements of these authors claiming the cancerous element to be secondary, may be replied: The same could be said of the shoot-producing tumors on Pelargonium and on tobacco did we not know experimentally that it is actually the infected tumor tissue which is the earlier and which has stimulated the normal tissues to develop. Moreover, which tissue is the earlier is a matter that can not be determined by mere observation of sections (Betrachtung des Wachstums—Wilms) but one to be worked out experimentally.

To condense results, I may say that during the past winter I have discovered that when the crown-gall organism (Bacterium tumefaciens) is introduced into the vicinity of dormant buds on growing plants atypical teratoid tumors are produced quite regularly. I have obtained these in Pelargonium, tobacco (2 speceis), tomato, Citrus, Ricinus, etc. Apparently what happens is this: The bud anlage are torn into fragments by the rapidly growing tumor and these fragments are variously distributed and oriented in the tumor where under the stimulus of the parasite they grow into abortive organs variously fused and oriented, some on the surface of the tumor, others in its depths. Surface fasciation occurs. Also in the depths of the tumors fragments of organs occur, lined by membranes bearing trichomes (hairs) and lying upside down and variously oriented and combined. The flower shoots, roots, and leaf shoots on the surface of such tumors vary greatly in number and size; often they are the merest abortions, and in that case there may be a hundred or more of them (leafy shoots or flower shoots) on a single tumor, especially on the Pelargonium. Even the largest and best developed surface shoots if they arise out of the tumor tissue and not from its vicinity are feebly vascularized and become yellow and dry up within a few months and often before the tumor itself decays. Such shoots never come to maturity, and frequently these shoots become invaded by the sarcoma, especially at their base, but otherwise their starved tissues are normally arranged. Immature fragments of what I have interpreted as ovaries and anthers also occur on the surface and in the depths of such tumors.

These teratomas when produced in leaf axils on the castor oil plant reach a large size and perish quickly, i. e., often within two months. Frequently in this plant the neighboring glands on the base of the leaf stalk are also invaded (within two or three weeks) and greatly enlarged. This is one of the striking results on Ricinus to which I would call special attention, since it is very suggestive of what often occurs in cancer in man; that is, of the malignant enlargement of lymph glands in the vicinity of a cancer. Following inoculations on the middle part of the leaf blade of Ricinus I have also traced a parenchymatic tumor strand down the petiole a distance of 11 centimeters. This was nearly circular in cross section, large enough to be visible to the naked eye, and composed of parenchyma cells. Corresponding to this were swellings on the surface of the petiole and bulgings into the petiole cavity, but no ruptured tumors. No teratoids were formed on the Ricinus leaves.

Daughter tumors are produced freely on tobacco if the inoculations are made early enough, and these often reproduce all the teratoid elements of the primary tumor,

[1] See Mechanism of Tumor Growth in Crown Gall. Journal of Agricultural Research, Government Printing Office, Washington, D. C., January 29, 1917.

e. g., daughter tumors 10 inches away from the primary tumor may bear leafy shoots. These secondary tumors, which have been seen both in stems and in leaves, are connected with the primary tumor by a tumor strand which is lodged in the outer cortex and is vascular, i. e., has the structure of a diminutive stem (stele).

What is still more astonishing, I find that I can produce these teratomas in the leaves of tobacco plants where no dormant buds are known to exist.[1] To get these results the leaves must be fairly young, i. e., plastic. They will then produce tumors where they are inoculated (needle-pricked) and many of these tumors will be covered with leafy shoots (tobacco plants in miniature). I have obtained 7 such teratomas from the blade of a single leaf, and 27 from the leaves of a single plant—too many to be due to Cohnheim's "cell rests." They must have originated, I think, from groups of plastic (totipotent) cells normal to the inoculated parts of the leaves and probably also present in many uninoculated parts of such leaves, if not in all parts. I have more recently produced them readily in geranium leaves and in the middle of cut internodes of both tobacco and Pelargonium by needle pricks introducing Bacterium tumefaciens.

How, then, can these phenomena be explained? The teratoids I have obtained being essentially like the embryonal teratomas in animals, I believe that in both plants and animals they must have the same origin, i. e., must arise from an identical chemical and physical stimulus. So far I have been able to explain the embryonal teratomas only on the assumption that in all animals and in all plants (except the simplest) certain widely distributed normally arranged cells or groups of cells, possibly all cells when very young and plastic, carry the potentiallity of the whole organism, which potentiality is not ordinarily developed on account of division of labor, but which comes into action when hindrances are removed, i. e., when the physiological control is disturbed or destroyed. We know that life must have begun so in unicellular plants and animals and there is no good reason why it should not have continued so in multicellular ones. Only we have not been accustomed to think of it in this way, yet there are many facts respecting regeneration of lost parts in both plants and animals which coincide perfectly with this view. Coinciding with this view as to the origin of embryomas in various organs, i. e., from groups of normal but very young undifferentiated or but slightly differentiated cells or groups of cells multiplying under a cancer stimulus, is the fact that I have been able to produce the teratomas in tobacco leaves only by inoculating very young leaves. When older leaves are inoculated they either do not respond or yield only the ordinary crown galls.

Respecting animal inoculations I might say that I have tried this organism on fish (brook trout) and in the eye cavity and elsewhere have obtained small nodules which in stained sections look very much like sarcoma, but in no case have I seen metastasis nor do I know that the nodules would not have been absorbed after a time. Most of my inoculated fish recovered or died early of septicaemias, some of which were due, I have reason to believe, to the crown gall organism. At least from the dorsal aorta of one of these sick fish we plated the crown gall organism in practically pure culture and with subcultures induced crown galls on healthy plants.

I may be permitted a few general remarks in conclusion, premising that this is the way the cancer problem looks to an experimental biologist.

With some praiseworthy exceptions, the cancer specialists of to-day, following the lead of the Germans and their English imitators, are lost in a swamp of morphology, and it is time that an entirely new set of ideas should be promulgated to rescue them from their self-confessed hopelessness.

When a pathologist can say: "Concerning the ultimate nature of neoplastic overgrowth we shall never have more than a descriptive knowledge," he has reached the

[1] See Journal of Agric. Research, Apr. 24, 1916, Pl. xxiii.

end of the road in his direction and the limit of pessimism. I do not care a rap whether I am called orthodox or heterodox, but I do care tremendously to keep an open mind and a hopeful spirit. One trouble with too many cancer specialists is that they are not biologists, whereas the cancer problem is peculiarly and preeminently a biological problem. These cancer morphologists have patiently cut and stained and studied hundreds of thousands of sections of tumors, fining and refining their definitions and distinctions and building up high walls of separation where nature has made none, all because they do not understand the plasticity of living, growing things. I do not mean to condemn the study of sections, but only to suggest that there are also other ways of looking at this problem, which is one of growing things. There is too much reasoning in a circle on the part of many of these writers, too much argument basing one assumption on another assumption as if the latter were a well-established and solid fact, too little clear thinking of a biological sort, too little first-hand knowledge of living plants and animals, too much dogmatism, too much orthodoxy, and not enough experimentation. Hence the pessimism and the discouragement.

Cancer research was born in Germany and has been prosecuted there more diligently than anywhere else in the world, and they have done wonders in the study of its morphology, but etiologically the best the Germans have been able to do has been to cover the whole situation with a cloud of obscurity. With a few uninfluential exceptions they have denied the parasitic nature of the disease and discouraged search for an organism, and in this pessimistic attitude they have been ably seconded by their English followers. These strong men, chiefly morphologists, have dominated the situation for a generation, but they have not explained cancer and they can not explain it, and they must now give way. Indeed, from Cohnheim to Ribbert there is not one of their arguments in opposition to the parasitic nature of cancer which is not as full of holes as a skimmer.

Listen to Ribbert in his last great book:[1]

Denn wenn auch durch Mikroorganismen knotige, tumorähnliche Wucherungen her orgerufen werden können, so handelte es sich doch stets nur um die Bildung eines entzündlichen Granulationsgewebes, das höchstens mit Tumoren der Bindegewebsgruppe eine gewisse Ähnlichkeit haben konnte (p. 378).

In other words, the most that parasites can do is to produce a granulomatous tumor superficially like a sarcoma.

Again he says:

Aber wenn das fremde Lebewesen die Zellen bewohnt, müssen diese notwendig geschädigt werden. Das folgt aus dem Begriff der Parasiten, der selbst erständlich der Zelle nur Nachteil bringen kann. Damit ist aber die den Tumor characterisierende Steigerung der Wachstumsfähigkeit der Zelle nicht vereinbar (p. 384).

In other words, when a parasite occupies a cell that cell must necessarily be injured. It follows out the very concept of a parasite that it can only bring injury to a cell, and the characteristic increase of cell growth in tumors is incompatible with this idea. Here as usual he just misses the point.

Ribbert ends his great book, of which "seine Entsehung" is its weakest part, although the illustrations are also to be criticized because they are all vague wash drawings when they should have been exact photomicrographs, as follows:

Das Karzinom entsteht auf Grund einer durch Epithelprodukte bewirkten die Differenzierung des Epithels vermindernden und sein Tiefenwachstum auslösunden subepithelialen Entzündung.

In other words, if I understand him, cancer is due to a sub epithelial inflammation induced by substances arising in the epithelium, which substances cause it (or which inflammation causes it) to be less well differentiated and to grow downward. This, etiologically is about as clear as mud.

[1] "Das Karzinom des Menschen sein Bau, sein Wachstum, seine Entstehung," Fr. Cohen, Bonn, 1911.

Wilms, also, at the end of his book,[1] sarcastically inquires:

Welches Bakterium soll wohl eine Keimblattzelle, Mesoderm- oder Mesenchymzelle producieren können, die dann embryonale Gewebe und Organanlagen bildet?

To which may be replied Bacterium tumefaciens, and probably others.

This is his additional and closing sentence designed to be a finality of invincible logic:

Wer diese genannten angeborenen Sarkomaformen als durch Bakterien erzeugt betrachtet, übernimmt damit die Verpflichtung, auch für die Bildung seiner eigenen normalen Gewebe und Organe eine bakterielle Infektion nachzuweisen.

To which may be answered: Very well, and why not? Since a bacterial organism does just that in the plant.

I believe these old ideas and assumptions must be sifted, turned and overturned, and many of them wholly rejected if we are to find the truth.

Cancer, according to my notion, is a problem for the experimental biologist and the bacteriologist. The morphologist has gone as far as he can go, and the energy of cancer research from now on must, I believe, be turned into new channels, if we are to expect results commensurate with the needs of humanity.

[For illustrations, drawn from photographs and photomicrographs, and confirmatory of statements here made respecting crown gall, consult "The Journal of Cancer Research," April, 1916, and, especially for the embryomas, "Bulletin of the Johns Hopkins Hospital," Sept., 1917."]

The CHAIRMAN. Are there any questions or remarks?

A DELEGATE. I am interested to learn what is the nature of the controls used in the work on trout. Do you find that no other infection will produce this kind of tumor in the trout?

Dr. SMITH. I can not say. I have not got in any of the inoculated trout tumors enough evidence to make me think that I have proved my case. The work is still going on. Until I can get metastasizing tumors in these animals and from them can produce the growth, I do not think I have made out my case. I do not know that I can make it out in animals, anyway, but the subject is interesting. I am working on lizards now, and perhaps after a time I may have some better evidence than this. But I have got here in plants what to my opinion parallels in a good many ways what takes place in man and many animals. I know it is due to an organism, but it does not kill the cell. It grows inside the cell and stimulates it to proliferate, and from that standpoint I think it well worth while to go on with the work.

Dr. RICHARD WEIL. I wonder whether Dr. Smith is entirely correct in saying that he does not get metastasis. Of course, he gets growth by extension, but then we know there is a school of human pathologists that believe human metastases are very largely due, if not exclusively—at least in a certain type of cases, e. g., the breast cancers with axillary metastases—to that mode of growth—i. e., extension with eventual destruction of intervening strands through connective

[1] "Die Mischgeschwülste," p. 275.

tissue proliferation, so that metastasis according to that belief is not caused by carriage of the toxin through the cells, but by actual proliferation.

That is certainly true in a considerable number of cases of metastasis. Whether it is true in all is an entirely different question, but I think there is no doubt that in many cases of human breast cancer we get just that method of extension that you get with eventual destruction of intervening strands. As far as I could make out from the slides, the growth was partly infiltrative, and I wish to ask whether there was true infiltration of the healthy plant tissue, whether the tumor throws out feeders, or whether it only extends from the center and destroys the surrounding tissues by pressure and so bursts out to the surface.

Dr. SMITH. In some cases it sends out invasive cell growths, at other times it exerts a purely crushing effect.

Dr. WEIL. Does the plant ever recover from the tumor?

Dr. SMITH. I think I can say that sometimes recovery occurs.

Dr. WEIL. Are they then immune?

Dr. SMITH. We have worked a good deal on that point. I felt a good deal more certain on the question of immunity some years ago than I now do.

Dr. H. R. GAYLORD. I should like to remind Dr. Smith of a very interesting occurrence in reference to this subject that he has probably forgotten. At the International Cancer Meeting, in Paris, there was presented to the Congress a new object for neoplasm study, a genuine neoplasm in plants, by a gentleman who stated that he thought it was of great value to human study because it could be demonstrated by all the criteria of neoplasms to be a genuine neoplasm. What he had done was this: He had this tumor in sugar beets, and he had proven by transplantation experiments that this tumor could be transplanted from one type of beet to another and grow by ingrafting. In other words, he took a tumor from a white sugar beet and transplanted to a red, or the reverse, and it grew from the transplant. He proposed that here was a very simple type of tumor which we could use for transplantation experiments. One of the criteria which he advanced to prove that it was neoplasm was that no one had ever been able to cultivate anything from it, and hence that definitely placed it in the neoplastic growths. He was very much surprised, we know, when he learned about Dr. Smith's growth. Dr. Smith had at that time accomplished the culture of this organism and had inoculated it. Dr. Smith might make more out of it, I think, than he does, because here was a tumor something like a Rous chicken tumor which was passed on before his work came out and was accepted as a type of neoplasm.

The CHAIRMAN. We will pass to the next paper, that of Dr. Gaylord on "Fish tumors."

CANCER PROBLEMS IN SPECIAL BIOLOGICAL GROUPS—FISH TUMORS—FURTHER OBSERVATIONS ON SO-CALLED CARCINOMA OF THE THYROID.

By HARVEY R. GAYLORD,

State Institute for the Study of Malignant Disease, Buffalo.

Our knowledge of the various types of neoplasms in fish has not been materially augmented since the articles of Marianne Plehn in 1906, 1910, and 1912. It is well known that various types of neoplasms are found in the teleosts, but for the purposes of cancer research the descriptions of neoplasms in lower animals serve only to extend our knowledge and to confirm our impressions regarding the widespread distribution of the neoplastic processes. Only when such tumors have been made the subject of experimental or more extended study is their significance great.

In fish the particular type of neoplasm which has been so studied is the so-called carcinoma of the thyroid in the salmonoids. Just as in other biological groups a certain type of neoplasm preponderates, as in mice carcinoma of the breast, and in rats and chickens the sarcomas, so the salmonoids have that type of neoplastic process which even in mammals bears a close relation to the problem of water supplies. Therefore, it is not surprising to find carcinoma of the thyroid in fish.

This disease was first described by Bonnet in 1883. Although this author did not recognize the nature of the disease, Scott, in 1891, described it as cancer, and Plehn, in 1902, recognized it as a neoplasm of the thyroid gland. In the same year it was described by Gilruth as epithelioma affecting the branchial arches. A comprehensive histological study based on some ten specimens of fish was made by Pick in 1905. Our interest in this subject began in 1908 with the description of conditions existing in a fish hatchery, in which hundreds of fish were affected. The disease was also studied by Marine and Lenhart, beginning in 1909, these authors considering it to be endemic goiter. Our own studies, covering a period of six years, were published in monograph form in 1914, and led to the following conclusions regarding the nature, distribution, and significance of the disease:

1. The disease known as gill disease, thyroid tumor, endemic goiter, or carcinoma of the thyroid in the salmonidæ, is a malignant neoplasm.

2. The disease occurs in fish living under conditions of freedom in populated areas.

3. When introduced into fish-breeding establishments it becomes endemic with occasional epidemic outbreaks.

4. Normal fish taken from the wilderness may be made to acquire the disease when placed in fish-breeding establishments where the disease is endemic.

5. The feeding of uncooked animal proteid favors and the feeding of cooked animal proteid retards the disease as compared with the uncooked. Feeding alone is not an efficient cause. It must be combined with an agent transmitted probably through the water or food, or both.

6. By scraping the inner surface of water-soaked wooden troughs in which the disease is endemic, an agent may be secured which from its action upon the mammalian thyroid when administered through drinking water is no doubt the cause of the disease in the fish confined in these troughs.

7. The agent is destroyed by boiling.

8. Fish in all stages of the disease are favorably affected in the direction of cure by the addition to the water supply in suitable concentration of mercury, arsenic or iodine.

9. The effect of mercury, arsenic, and iodine in carcinoma of the thyroid in fish and the subsequent positive experiments with metals in mammalian cancer are probably the expression of a therapeutic relation of these elements to carcinoma.

10. Certain species of the salmonidæ have an almost complete natural resistance to the disease.

11. Certain lots of fish of susceptible species show a high degree of immunity to the disease.

12. Spontaneous recovery occurs in a considerable percentage of individuals.

13. Removal from ponds in which the disease is endemic to natural conditions, or a change to more natural food, increases the percentage of spontaneous recoveries.

14. Spontaneous recovery appears to confer a degree of immunity against recurrence.

15. The percentage of spontaneous recoveries in the early stages of the disease appears to be higher than in the later stages of the disease.

16. The incidence of the disease increases with the age of the fish, at least up to five years.

17. Thyroid enlargement and changes presenting at the end of five months a picture of diffuse parenchymatous goiter were induced in mammals by giving them water to drink in which had been suspended scrapings from troughs in which the disease was endemic. Control animals which received the same water boiled failed to develop thyroid changes. That these enlargements and changes are the first stages in mammals of the same disease which occurs in the fish inhabiting the troughs from which the scrapings were obtained is an inference which we believe further experiments will justify.

18. The disease is endemic in a very high percentage of all trout hatcheries in the United States.

19. The occurrence of the disease in wild fish, its introduction into fish-cultural stations, its localization in certain troughs or water supplies, the method of its spread, its transmission to mammals, the efficacy of three well-known inorganic germicides in the treatment of the disease, the destruction of the agent by boiling, the phenomena of spontaneous recovery and immunity, strongly indicate that the agent causing the disease is a living organism.

20. No evidence has yet been produced to indicate the direct transmission of the disease from individual to individual.

21. In many of its phases the disease is identical with endemic goiter. As there is no line of demarcation between what is called endemic goiter and what we believe we have clearly shown is cancer of the thyroid, we hold that endemic goiter and carcinoma of the thyroid in the salmonidæ are the same disease.

Since the publication of these conclusions, certain new facts have been disclosed which serve to extend or strengthen some of our conclusions in regard thereto. That the disease is widespread geographically is indicated by reports we have received of its occurrence in India. T. Southwell, director of fisheries for Bengal, Bihar, and Orissa, wrote us in 1914 and later sent us specimens of rainbow trout taken in the hill waters in the vicinity of Naini Tal with visible thyroid tumors. These proved on microscopic examination to be thyroid carcinomata of the usual type. Facts pertaining to this observation have since been published by Southwell with two excellent illustrations in the records of the Indian Museum.

In the literature of the subject there is but one reference to the occurrence of visible thyroid tumor in salt-water fish, and this only in Salmo salar Linnæus, the Atlantic salmon. As these fish at certain times ascend the fresh-water streams, they are not strictly salt-water fish. It is, therefore, of great interest to learn of the existence of the disease in four examples of sea bass, Serranus, in two species. These fish were found in the Naples aquarium by Dr. Paul Vonwiller and will be later published in detail by Marsh and Vonwiller. The growths are in general like the process in the salmonidæ but are not so advanced. Colloid is found in all sections of the tumor. The epithelium is in all stages from low cubical to high columnar, and not greatly infolded, but presents an appearance of adeno-carcinoma. In Serranus there is very little evidence of infiltration and no metastases are demonstrable, as only the heads of the fish are available for investigation. These fish were always in sea water, and they were fed

exclusively on marine fish, which is said to prevent thyroid overgrowth. This is the first observed instance of thyroid tumor in salt-water fish outside the salmonidæ.

Still more striking is the observation of Cameron and Vincent of the occurrence of thyroid tumor in an elasmobranch, squalus. Squalus is a dogfish, or small shark. These authors, in the examination of 217 specimens of dogfish from the Pacific coast, found a thyroid which was enlarged to about three times the usual size, and the gland instead of being leaflike and flat as normally, was pear shaped and nodular. The enlarged gland contained cysts and under the microscope cystlike dilatations of the alveoli with cell proliferations projecting into them. There were areas of normal vesicles containing colloid in parts of the gland, but the alveoli in the more characteristic portions were filled with solid masses of cells. In some places all alveolar structure was lost, the growth being made up of irregular masses of cells. The general appearance of the growth was adenomatous, but in certain regions infiltration of the interstitial tissue was marked. The picture described by these authors is characteristic of the disease in the salmonidæ. The point of especial interest is that the thyroid in squalus is an encapsulated gland. Besides this one example of gross enlargement of the thyroid in squalus, these authors describe two specimens from a group of 12 examined later which show distinct pathological changes on microscopic examination. In these glands large portions of the thyroid were devoid of colloid, the vesicles being entirely filled with epithelial overgrowth. The sea water of the strait of Georgia, where the squalus was obtained, is about two-thirds normal ocean salinity, and doubtless two-thirds normal marine iodine content, but this is much above the concentration of iodine which in fresh water reduces thyroid hyperplasia.

From these observations the evidence which has been collected of the existence of carcinoma of the thyroid in fish living under conditions of nature, and far removed from questions of domestication, overfeeding, overcrowding, etc., strengthens the conclusion that the disease is not the result of artificial propagation. The occurrence of the disease in fish whose normal habitat is sea water bears rather strongly upon that theory of thyroid hyperplasia which attributes it to deficiency of iodine in the food or environment. In fact so far as fish are concerned the similar results obtained with mercury and arsenic would seem to conclusively show that idoine acts in a way similar to the metals, and not by supplying a deficiency of iodine in the gland. The observation that the feeding of vegetable food, cooked proteid, or chopped sea fish, or so-called natural food, such as maggots, bugs, etc., retards the progress of the disease in hatcheries, and that the feeding of uncooked animal proteid is not the cause of the disease but a contributing factor, has been strengthened by the observation of the occurrence of the disease in trout fed on cooked vegetable food. These fish came from a commercial trout hatchery in Pennsylvania. The first food of these fish as fry was beef liver for about two months. Then a mush made from wheat flour is added to the liver and is gradually increased in relative proportion until during the next four months all liver is eliminated. Subsequently only cooked flour mush is fed to these trout. They grow slowly, mature and breed, and are sold for table use at probably a record price for commercial trout. They nevertheless acquire thyroid tumors; in yearlings and older fish. The tumors are small, and a small per cent of fish are affected. Microscopically, most of the typical appearances of carcinoma in the salmonidæ are seen. This is cancer in fish. The occurrence of the disease in Serranus, sea fish fed exclusively upon marine fish food, also strenghens the conclusion that feeding is not the essential cause of the disease.

The observation that mercury, arsenic, and iodine, when introduced, even in small amounts, into the water containing fish with thyroid tumors, bring about a marked diminution in the size of these, develops increased significance in the light of recent experiments reported by McCarrison. This author has studied the prevalence of goiter in the Lawrence Military Asylum for children at Sanawa. In this institution there are about 500 male and female, European and Anglo-Indian children. About two-

thirds of the children are of pure European descent, the remaining one-third being of mixed parentage. The asylum is located at about 6,000 feet in the lower ranges of the Himalayas. A careful study of the records in this asylum, which extended over some 15 years, showed that the incidence of goiter, with the exception of a few years, was about 20 per cent of the inmates. McCarrison finally traced the source of the endemic to the drinking water, which was in part rain water and in part spring water. Both sources of supply were open to fecal contamination and showed abnormally high bacterial content. Beginning April 19, 1913, McCarrison undertook the experiment of sterilizing the water by chemical means in the boys' school and barracks, while for control purposes the water supply of the girls' school and barracks remained as before. At the commencement of the experiment, there were 284 boys in the school, of whom 57 were goitrous. There were 216 girls in the school, of whom 57 were goitrous. On the 25th of November, 1913, when the experiment was completed, the number of cases among the boys had been reduced to 27, whereas among the girls there was an actual increase of cases above the 57 first recorded. Partial sterilization of the water was carried out by the use of iodine in the form of potassium iodide and iodate. The amount of iodine employed equaled 1 part in 70,000. This method was used to purify the water until the 2d of July, 1913, midway in the experiment, and from July 3 on, chlorine was largely substituted for iodine, with the continuation of the results observed in the first instance.

In the latter part of the experiments the amount of iodine per parts of water was reduced to 1 in 911,000. This is still five times as great a concentration as we used in treating goiter in fish by the addition of iodine to the water. McCarrison considers the question of whether the iodine acts in this case as a purifier of water, especially as a germicide, or whether its action in diminishing the number of cases of goiter is to be attributed to its supposed physiological action upon the gland. As in the treatment of goiter McCarrison has obtained equally efficacious results with thymol, he is not inclined to attribute to iodine a distinctly physiological action in the treatment of goiter.

McCarrison's experiments do not conclusively show that the iodine works by destroying an agent in the water supply. It is still possible that the iodine acts as a germicide in the individual drinking the water. It is to be regretted, that McCarrison did not entirely substitute chlorination of the water for treatment, with iodine. As a confirmation of the results obtained with iodine by Marine and by ourselves, his work indicates a very valuable application of this method in the practical treatment of goiter in human beings.

The CHAIRMAN. If there is no discussion, we will proceed to the next paper, by Dr. Lambert, on "Tissue culture in cancer."

TISSUE CULTURES IN CANCER.[1]

By ROBERT A. LAMBERT,

Department of Pathology, College of Physicians and Surgeons, Columbia University, New York City.

ABSTRACT.

The cultivation of tissues in vitro forms a very valuable addition to our methods of investigating cancer problems. Factors may be introduced and controlled to an extent not possible in experiments upon the living animal. One may observe directly the

[1] The committee on publication regrets that, owing to the absence of the writer in South America, only this abstract of Dr. Lambert's paper can be printed.

division of cells and follow succeeding generations of cells under variously modified conditions of life.

There are limitations to the method. Not every cancer cell or normal tissue can be cultivated, and when cultures are successful growth is by no means comparable to that observed in cultures of bacteria. Some tissues merely survive. Human tissues offer special difficulties, although modifications in technique have enabled us to maintain an active multiplication of human cells for more than a month. It is probable that growth may be kept up indefinitely.

The method of tissue cultures has been used by us chiefly in studying the nature of cancer immunity, and in carrying out comparative studies upon the biology of cancer cells and normal cells. Further evidence has been obtained to show that cancer immunity is not a serum immunity, that circulating antibodies for the cancer cell do not exist. Tumor cells grow actively in the plasma of animals which are naturally or artificially highly resistant to tumor inoculation. They even grow, as do also normal cells in the plasma of certain foreign species, except when such animals have been immunized by suitable injections against the tissues of the species to which the tumor belongs. In other words, cytotoxic immunity, in contrast to tumor immunity, is readily demonstrable in tissue cultures.

Interesting differences are observed in the behavior of cancer cells and normal cells in cultures, especially when the cells are subjected to the action of certain harmful agents. Cancer cells, particularly sarcoma, grow very actively in the primary cultures, but continued propagation through subcultures is difficult, often impossible. The reverse is true of normal connective tissue cells which become more active in subcultures. This observation is probably significant, indicating either that tumor cells are less hardy or that in cultures some necessary substance is not sufficiently supplied.

To some physical agents, such as cold, tumor cells (mouse and rat sarcomata) appear to be more resistant than normal tissues. To other injurious agents, notably heat, the neoplastic cell is clearly less resistant. Recent experiments indicate that these results apply also to human tissues. It is suggested that the problem of the therapy of cancer may be profitably attacked by this method.

Efforts have been made to stimulate in various ways the growth in vitro of cells, both normal and malignant. Work in this direction is promising, and is undoubtedly of greatest importance. The author has been unable to confirm some of the positive results reported by others. Some substances which stimulate the growth of cells in the body appear to be without effect in cultures.

Finally, it is perhaps interesting to note that normal cells grown for a long time outside the body do not develop as the result of their freedom from the restraint of the organism any tendency to malignant lawless growth. This is shown by the entirely negative results following the inoculation of subcultures actively growing of normal connective tissue cells.

The CHAIRMAN. Before proceeding with the discussion I propose that we hear Dr. Burrows's paper, which is of a similar character, "The tissue culture in cancer," by Montrose T. Burrows.

THE TISSUE CULTURE IN CANCER.[1]

By MONTROSE T. BURROWS,

Pathological Laboratory, The Johns Hopkins University, Baltimore, Md.

Cancer considered in its general aspects is a condition, although unique, which must be understood only by the use of those same methods by which we are to even-

[1] Abstract of paper.

tually understand normal and other pathological processes. The important problem in pathology and in biology is the structure and metabolism of normal body cells. The question in cancer is whether the cancer cell is a normal cell responding to a peculiar environment or whether it is a cell whose metabolism is such that it can grow in an environment where other cells can not show these changes.

At one time it was supposed that the cycle of the life of the organism was the cycle of the life of the cell. At the present time, however, this particular view has been largely discarded and it has come to be considered that the body is not only controlled by its cells but that the cells are likewise controlled by the body. There is a mutual interrelation between the whole and its minute parts. Each and every activity of the cell is a response on its part to some external stimulus. Each and every activity of the whole is the result of the coordinated activity of its parts. The cessation of the growth of many cells at maturity does not represent a loss of the property of these cells to proliferate, but it is the result of some kind of a change either in the organization of the cell or in the parts about it.

Although it has been assumed that this peculiar type of regulation of growth and other changes in the body cell is the result of peculiarities of their structure and metabolism, and that it must be solved by direct analysis of the mechanisms peculiar to each of the various activities of these cells, up to the time of the development of the tissue culture method no means for such direct analysis had been devised. The tissue culture method has become important in cancer as in the study of normal and other pathological processes in that it allows one to study directly the reactions of these various cells in a restricted and analyzable environment.

During the last few years the author has studied by this method several different kinds of normal and cancer cells. Through this study he has been able to demonstrate directly that the normal cells of the organism are essentially fluid systems and that the organization peculiar to their various activities, such as growth, movement, differentiation, function, etc., are differential surface tension phenomena, regulated by the organization of the environment and the peculiar properties of certain of the substances formed in their oxidation reactions. The organization peculiar for each of these activities is not a cellular but a tissue organization. Thus it is seen how these cells may under the influence of changes in their environment undergo changes in form and activity.

A further careful study of oxidation in these cells has been made. Oxidation in these cells is a simple, incomplete chemical reaction. CO_2 and another or other substances are formed. Certain of these compounds formed are insoluble in the circulating body fluids, serum, salt solution, etc., but soluble in various body colloids, such as fibrin, dead cells, etc. In the presence of food and oxygen this oxidation reaction can continue only so long as these products remain below a certain concentration. When this concentration is attained about the cells all activity ceases. For growth to take place in these cells a special mechanism for removing these products must be available. That is, it can take place only when the cells are brought into contact with certain colloidal materials having the property of absorbing these substances and it continues until their concentration in these colloids reaches a certain concentration; then an equilibrium is established. Thus, we can see how the coaguable exudate in the wound forms the stimulus for growth and how growth ceases at the establishment of continuity of the part or how it fails through a failure of the formation of the exudate.

A careful study of the nail shows that it has a special mechanism for supplying colloidal materials and removing them continuously from the growing cells. The rhythmically contracting heart muscle cell has an electromechanical structure capable of splitting these substances into simpler compound which are soluble in the circulating body fluids. The energy is transformed into work in these cells through the fact

that the primary oxidation products decrease surface tension while their split products increases it.

Cancer cells have not been found to be different from actively growing normal cells. The study of them has, however, been so far limited.

The CHAIRMAN. There is an additional paper by Dr. Clowes, on "The mechanistic theory of cancer," which is very similar in its contents to the present papers. The papers are very interesting and I hesitate to cut them short, but I think the time is passing fast and we have to be as brief as possible in these communications.

A MECHANISTIC THEORY OF CANCER.

By G. H. A. CLOWES,
Research Hospital, Buffalo, N. Y.

While investigating 12 years ago the conditions under which spontaneous recovery from cancer occurs in mice, and the phenomenon of immunization against subsequent transplantation of the same material, we had an opportunity to confirm Beebe's observation that the saline constituents of tumors appear to bear a direct relation to their speed of growth. We carried out detailed analyses on upward of 80 carefully controlled mouse tumors and noted an extremely high K and low Ca content associated with rapid growth and exceptional virulence of these tumors, whilst a relatively low K and extremely high Ca content was associated with relatively slow growth and tendency to spontaneous recovery on the part of the tumors.

While analyses carried out on such a small amount of substance are necessarily somewhat inaccurate, it is interesting to note that in the large majority of cases the speed of growth and probable virulence of a tumor could almost be determined by reference to the analytic data. A high K content is commonly associated with rapidly growing embryonic tissues and a relatively high Ca content with stationary, retrograding, and senile tissues. But it appeared desirable to seek some further explanation for the variations exhibited in these mouse tumors, particularly the mechanism underlying the mobilization of Ca in those tumors in which the growth was inhibited and spontaneous recovery occurred. The data appeared to bear some relation to experiments being published at that time by Jacques Loeb and his associates on antagonistic effects exerted by salts of monovalent cations against salts of divalent cations, particularly in so far as they might apply to the problem of increased or diminished permeability of the protoplasmic film of the cancer cell, and consequent accelerated or diminished intake of foodstuffs and building materials capable of causing either normal or pathological cell proliferation.

Some years later while confirming and elaborating the work of other investigators on the so-called antitryptic reaction which occurs most markedly in cancer and in pregnancy, I was able to demonstrate that the amount of these substances produced in the blood appeared to bear a direct relation to the speed of growth of either a tumor or a fetus, to diminish rapidly following an operation for cancer or the birth of a child, only to increase once more with any subsequent recurrence of the malignant condition or in any subsequent pregnancy. From an investigation of the extent to which the substances in question were influenced by treatment with organic solvents, by heating and the action of physical agents, I concluded that they represented products of the destruction of lipoids and other fatty materials which are believed to play an important rôle in the protoplasmic film or membrane, and subsequently Jobling, as a result of fractionation experiments with organic solvents, came to the conclusion that the substance causing the so-called antitryptic reaction in cancer is actually a

simple, water-soluble soap. The production of increased proportions of soluble soaps in the blood appeared to support the conclusion of Shaw-Mckenzie that an increased lipase activity is to be noticed in cancer and suggests the possibility that the mobilization of Ca is a protective measure calculated to counteract the increased permeability of the protoplasm resulting from the disintegration of the protoplasmic film, the soluble soaps produced being transformed into insoluble Ca soaps.

There was, however, no satisfactory explanation for the phenomenon in question until Bancroft made the observation that water-soluble soaps, like Na and K oleate, when used as emulsifying agents for oil and water, promote the formation of emulsions consisting of globules of oil dispersed in water, like cream, while soaps like Ca and Mg oleate, which are insoluble in water but soluble in fats, when used as emulsifying agents promote the formation of emulsions in which globules of water are dispersed in oil, like butter.

In a paper published in 1913 I was able to demonstrate that emulsions of oil dispersed in water may be transformed into emulsions of water dispersed in oil by simply shaking with salts of Ca, while the transformation in question may be prevented or the reverse transformation effected by shaking with alkalies, etc. Now, since a phase reversal of this type represents a transformation of a system analogous to islands surrounded by water which is freely permeable to water, into one analogous to lakes surrounded by land which is impermeable to water, it is obvious that by simply varying the proportions of alkalies and salts of monovalent cations, on the one hand, and of di and tri valent cations on the other hand, it is possible to prepare a physical system having any desired degree of permeability.

A careful investigation [1] of the effect exerted by various electrolytes on interfacial soap films by means of the drop system has demonstrated that the proportions in which given salts exert an antagonistic effect upon one another in these purely physical systems correspond exactly with the proportions observed by Loeb, Lillie, Osterhout, Matthews, and other investigators who have devoted their attention to the phenomenon of antagonistic electrolyte effects on cell protoplasm. From Osterhout's observation that NaCl diminishes the resistance of the tissues of certain marine organisms to the passage of an electric current and salts of Ca exert the reverse effect increasing the resistance, while properly balanced solutions of NaCl and $CaCl_2$ exert no effect upon the resistance, it may be concluded that antagonistic electrolytes function in virtue of their capacity to induce variations in permeability of the tissues, substances of the one type causing an increase and substances of the opposing type causing a decrease in permeability. The close parallel between the nature and proportion of salts capable of exerting antagonistic effects in such purely physical systems as emulsions and the drop system on the one hand and living cells on the other suggests the extreme probability that the mobilization of soaps of monavalent cations in rapidly growing normal or cancerous tissues bears a direct relation to increased permeability with resulting increased intake of foodstuffs, and that the mobilization of Ca in stationary or retrograding normal and cancerous tissues bears some relation to a reaction on the part of the system against such increased permeability and an attempt to induce a compensatory effect.

The question now arises as to how such changes in permeability could be induced in pregnancy or cancer, as to what forces might possibly cause abnormal lipase activity or stimulate the lipase normally present or otherwise lead to increased soap production or increased proportion of salts of monovalent cations as compared with divalent cations, thus leading to an increased dispersion of the constituents of the external protoplasmic film and a consequently increased permeability of the protoplasmic

[1] Protoplasmic Equilibrium, by G. H. A. Clowes, Journal of Physical Chemistry, vol. 20, p. 407. Antagonistic electrolyte Effects in Physical and Biological Systems, Science, vol. 43, p. 750.

system to water borne foodstuffs capable of affording those building materials necessary for cell proliferation. In experiments not yet published we have noted marked acceleration of lipase action on fats induced by a variety of agents which may well be present in the body under both normal and pathological conditions.

It is well known from the experiments of Loeb on artificial parthenogenesis and of Calkins regarding the conditions under which paramecia may undergo division without the intervention of the sexual cycle, that slight variations in the concentration and proportions of certain normal salts may induce cell division reaching many hundred generations, a figure far in excess of that required to account for cancerous development as it occurs in human beings.

While it is perfectly possible that toxic agents derived from parasites may under certain conditions play an important rôle in inducing changes of the type suggested, the fact that physicochemical phenomena associated with cancer and pregnancy bear such a striking resemblance to one another as indicated by a large variety of blood reactions, raises the question as to whether both conditions may not be induced by similar variations in the colloidal equilibrium of the protoplasmic system. Cell protoplasm apparently represents a colloidal chemical adaptation to salts and other chemicals originally present in the environmental medium in which protoplasmic material first came into being. This accounts for the extraordinary resemblance in the proportions of certain electrolytes in sea water and the blood of mammals. With marked variations in diet the cell is obviously forced to exert an ever-increasing selective effect in order to maintain its equilibrium and ultimately the production of abnormal, suboxidized, metabolic products exerting a cumulative effect taken in conjunction with an abnormal saline environmental medium may well lead to changes in colloidal equilibrium in the protoplasmic cell structure of those tissues which exhibit an hereditary weakness or predisposition to cancerous development.

Peyton Rous's observation that the agent inducing chicken sarcoma may be filtered through a Berkefeld bougie, and the observation[1] of Simpson and the writer that the agent in question may under suitable conditions be obtained from the filtered blood plasma of cancerous chickens, is in no sense incompatable with the mechanistic conception outlined above. It may be demonstrated by experiments with purely physical systems that under given conditions of saline equilibrium an agent capable of exerting a profound effect upon the surface tension of dispersed colloids may be passed through a bougie and may subsequently induce a cycle of changes resulting in the production of a further proportion of the substances in question and subsequent further development in the same direction, the process being analogous to an exothermic chemical reaction like an explosion as contrasted with an endothermic reaction.

While biologists have generally believed that the temporary intervention of physical or mechanical agents could not induce permanent changes in protoplasmic equilibrium which would find expression in permanent changes many hundreds of generations after the removal of the cell from the influence of the agents in question, it must be recognized from the experiments of Ehrlich regarding the action of certain chemicals on trypanosomes and from the experiments referred to above that changes of this type sufficiently permanent to account for cancerous proliferation may well be induced by chemical or physical forces. In the present state of our knowledge it is impossible to determine whether a parasite plays any direct or indirect rôle in the production of cancer, but it is perfectly conceivable that the filterable agent obtained by Peyton Rous bears a direct relation to substances isolated from the tissues by Robertson and others which, even when employed at extreme dilution, are capable of inducing membrane formation in the eggs of certain marine organisms.

[1] Am. Mid. Assoc. Vol. 64, p. 1525.

The CHAIRMAN. These papers are now open for discussion.

Dr. J. BRONFENBRENNER. The paper which Dr. Clowes presented yesterday broadens out a good many questions in immunity. I have come to the conclusion that at least a part of anaphylaxis due to extra-cellular phenomena has been plainly proven in our experiments to depend on physico-chemical changes in these media. If the experiments of other investigators are correct, it is easy to show that by dissolution of lipoids. I was able to produce the phenomenon by merely passing vapor through the serum. By means of this method I was able to dissolve lipoids and split up the particles which probably are constructed in the manner illustrated by Dr. Clowes. The proteolytic enzyme digests the protein of the serum and forms very toxic products. I do not mean to say that all of anaphylaxis is taking place in the blood serum, as I am sure that essentially the same elements are present in the cells as in the serum, and that a certain amount of proteolysis must be taking place also in the cells. I would like to have Dr. Clowes explain the fact that combination of antigen and antibody seems to be doing the same sort of work as a combination of calcium and sodium, or calcium and potassium; that is to say, how does it happen that in certain quantitative limits a combination of specific antigen with its corresponding antibody does break the film around the protein molecule and liberates substances within? That combination of antigen with antibody would thus break up the outer film and then liberate the substances. That the surface tension is very essentially involved in the phenomenon we have proven in experiments. There is no doubt that the phenomenon is entirely physico-chemical, as we tried to emphasize yesterday.

Dr. E. F. SMITH. I wish to say a word about some work that has been done in the Department of Agriculture on the effect of removal of calcium from balanced solutions in which plants are grown. Dr. Rodney Drew and Mr. Bartlett made a long series of experiments by growing certain plants in balanced solutions from which calcium had been withdrawn. The result seems to be that the membranes become very permeable and fluids or substances pour out from these plants into the solution as soon as we remove the calcium. You add the calcium and the membrane becomes more impermeable. The results were measured electrically by the electrical apparatus and I think that there can be no doubt about that result. As to the occurrence of potassium in these rapidly growing tumors, I think it may be true in all life that young, actively growing parts had more potassium than the older parts. It is certainly true of some plants that young actively growing normal tissues have more of potassium than of cal-

cium. As the growth becomes more mature the amount of potassium decreases and the amount of calcium increases.

The CHAIRMAN. Will you close the discussion, Dr. Clowes?

Dr. CLOWES. The experiments which Dr. Smith mentions have also been made by Osterhaut, showing that sodium chloride will lower and calcium will increase the resistance of certain marine substances, laminariæ, etc. He has tried it out, and his curves with all known elements correspond with my own curves, which I have shown here. Furthermore, at a meeting in Boston recently, he said he had curves to duplicate my own which he had not yet published.

As regards the question of antigen and antibody, I do not think it belongs in this discussion. I have already produced results, as I explained, in which I have duplicated with antigen and antibody in various ways these very same effects, producing an increase in permeability, in the drops, by means of an antigen-antibody combination, and counteracting them by means of calcium in the specific way we mentioned when dealing with hay fever and other anaphylactic phenomena.

As regards the question of enzymes, I look upon enzymatic effect as simply the promotion of contact between the otherwise non-missible phases, thus permitting constituents of one phase to exert chemical or physical effects on constituents of the other phase. If this effect is dispersion, it is simply a lowering of surface tension, whereby the particles more readily fly apart; if aggregation, a heightening of surface tension. And, of course, what takes place is that the dispersion or breaking up of any stabilizing film around the cell will render the passage of substances contained in that cell more easy.

The CHAIRMAN. The next paper is by Dr. Wood.

RADIUM IN EXPERIMENTAL CANCER.

By FRANCIS CARTER WOOD,

Director of Cancer Research, George Crocker Special Research Fund, Columbia University.

While there are many interesting biological problems connected with the action of radium on tissues, we are concerned chiefly in determining its value as a therapeutic agent in neoplasms of man. It is, however, extremely difficult to apply the necessary scientific criteria to the investigation of human tumors, as it is impossible always to obtain satisfactory specimens for microscopical examination, especially if the tumor is in the internal organs; the danger of overtreatment with resulting severe burns is always imminent; and, finally, we are, in this country at least, unable to obtain any satisfactory proportion of autopsies on persons dying from any cause after treatment. The result of this unsatisfactory condition is that the medical literature is filled with practically worthless reports of the effect of radium on tumors. In very few of these reports is any statement made as to whether the tumor was examined microscopically, or whether the patient was kept under observation for a time sufficient to warrant any opinion as to the ultimate cure. In fact, many cases have been reported a few weeks

after treatment, when any opinion is absolutely valueless, and many of the reports which are published as showing that benefit has resulted from the treatment concern patients who are already dead from the disease. Such publications are worse than useless, for they are misleading as regards the real therapeutic value of radium. It is much more important for us to know, not the number of successes, but the number of failures and their proportion to the successes.

It is my opinion that the percentage of cures of cancer—and this opinion is based not only upon personal experience, but upon a wide survey of the literature of the last 10 years—is extremely small and largely confined to certain groups of tumors, among them the basal-cell tumors of the face, the epulides of the jaw, the giant cell sarcomata of the long bones, the adenocarcinomata of the uterine body, and certain lymphosarcomata. All of these tumors, as is well known by those of sufficient experience, either may undergo a spontaneous disappearance, at least for such periods as would warrant the diagnosis of a clinical cure, or are curable in some instances by the mere removal of the main mass; although later, especially in the case of the lymphosarcomata, a fatal recurrence is frequent. For these and other reasons it is necessary to turn to spontaneous or implanted tumors in animals as a means of scientifically testing the therapeutic value of radium.

First, it is important to know what the minimal lethal dose of radium is for cancer cells outside of the animal; the viability of the treated cells being tested by inoculation after treatment. Such experiments have shown that when the alpha rays are removed by suitable filters, 100 milligrams of radium element at a distance of approximately 5 millimeters require one hour to kill carcinoma or sarcoma cells of the mouse or rat in vitro. If the filter used is of sufficient thickness to remove all of the beta rays also, the time required is increased seven or eight fold. The experiments have shown that in order to produce these effects no other factors are in play except the amount of radium, the length of the exposure, and the distance between the radium and the tumor cells. This furnishes, then, a lethal coefficient which can be plotted as a simple rectangular curve and by means of this anyone can determine the exact length of time required to kill a cancer cell at a given distance with a given amount of radium. The experiments have shown also that sublethal doses slow the growth of cancer cells, while still smaller doses stimulate, and they confirm the observations made on human beings, that with sublethal doses healing of a carcinomatous ulcer may be produced, while the cancer itself keeps on growing in the lower layers and is either slowed, stimulated, or uninfluenced, depending upon the amount of radiation reaching the cells.

These phenomena explain the sometimes astonishing increase in the growth rate which has been observed after the treatment of human tumors with insufficient radium, and also explains the very late recurrences which have occasionally been noted after treatment with radium or X-ray. Some of these recurrences have occurred some years after treatment, the cells remaining quiescent in the tissue for that period.

Second, it is necessary to find the lethal dose of radium for cancer cells when these are left in the tissues with their full blood supply, and experiments carried out to determine this have shown that the amount of exposure required to produce the same results is considerably greater, in fact, nearly double the amount required in vitro. Evidently there is some interference with the destructive action of the rays caused by the renewal of the cell substance through the circulation.

Third, it is important to find the lethal coefficient for human cancer. So far as clinical experience goes, the lethal death point of animal and human tumor cells is very nearly the same, and there is no reason to think that there should be much difference. Inasmuch as it is impossible to inoculate human cancer cells after treatment, it has been necessary to grow them in culture, a procedure which is attended by many complications and technical difficulties, but which is now in progress in the Crocker laboratory. There is, however, another factor which appears in the

treatment of human material and that is, that it is probably not necessary, in order to produce a cure, to kill all of the cells; but that if a certain amount of radiation is given, the closure of the blood vessels by the endarteritis which the radium produces and the new growth of connective tissue induced as a repair process following the arterial thrombosis and as a direct effect of the irritating action of the radium on normal tissues, may effect a choking of a certain amount of the carcinoma, and produce a temporary or symptomatic improvement of very considerable extent. This may explain the fact that in some cases less exposure is needed to cure a small human cancer of low virulence than to kill a mouse cancer in vitro.

Experiments in treating primary tumors of animals and the results of treatment of human cancers of high malignancy have, however, shown that in those portions of the growth where the cells of the tumor are in contact with normal structures it is extremely difficult to destroy the healthy blood vessels and, therefore, to influence the shell of carcinoma tissue, which still remains, even though the main mass may have disappeared under the influence of the radium. It is from this shell of actively growing neoplasm, thin as it may be, that recurrence takes place, and this is the difficult phase for any permanent cure. It is generally stated in textbooks and held by many workers that a cancer cell is more susceptible to any destructive agent than is a healthy cell. This is very doubtful; it is probable, though not as yet decisively shown, that a rapidly growing epithelial cell is just as susceptible to the action of radium as a rapidly growing cancer cell derived from the same tissue. We must always remember that the blood vessels in cancer tissue are thin walled and without vasomotor nerves, and that they are very easily injured, or even destroyed, by toxic agents, such as bacterial toxins, which have been widely used in the form of the toxins of streptococcus and prodigiosus, by the action of colloidal metals, and even by adrenalin, which simply raises the blood pressure and causes hemorrhages throughout the tumor, probably by mechanical tearing of the delicate walls of the capillaries. Following any of these treatments there may be a central necrosis of the tumor with a loss of a very considerable portion of the mass; but ultimately recurrence takes place from the periphery.

In a very few cases unquestionaoly, and especially in tumors of the variety mentioned in the first part of this paper, the balance between the tissues and the new growth is so delicate, so easily overthrown spontaneously, that the healthy tissues may be victorious and all the cancer cells ultimately destroyed, but in the vast majority of virulent tumors this delicacy of balance does not exist; the cancer cells do not induce any reaction against themselves by their growth, or at least sufficient reaction to be of any therapeutic benefit, and despite a certain amount of central sloughing a continuation of growth is to be observed with ultimate extension of the tumor, the formation of metastases, and the death of the patient.

To a certain extent we are able to judge the type of tumor which may be influenced with radium. That is, any tumor rich in giant cells, especially of the myeloplax type, as epulides of the jaw and the central sarcomata of the bone epiphyses, is more easily influenced than any other type of sarcoma. The basal-cell epitheliomata of the upper portion of the face, and the adenocarcinomata of the body of the uterus, which are of low invasive power and not infrequently cured by simple curettage, are especially susceptible to radium and may therefore be influenced, but exceptions occur in the experience of everyone who has used this agent, and therefore, until we have much more knowledge of the biology of these tumors, it is impossible to guarantee that radium will in all cases favorably influence them. Until we know exactly what radium will do it is improper to apply it to operable tumors, and we ought, therefore, in our experiments on human beings still to use only such tumors as are decided to be absolutely inoperable.

The CHAIRMAN. I take pleasure now in announcing Dr. William Duane, the writer of the next paper.

RADIUM IN THE TREATMENT OF CANCER.

By WILLIAM DUANE.

The Cancer Commission of Harvard University.

Soon after Röntgen discovered X rays in 1895, Becquerel, of Paris, found that certain urnaium salts produced rays similar to them. About two years later Monsieur and Madame Curie succeeded in extracting from pitchblende two new elements, polonium and radium, which possess this property of emitting peculiar types of rays to an exceptionally marked degree. In 1899 Danlos commenced studying the effects of radium rays on certain skin lesions. Thus radium therapy had its beginning at the close of the last century, and is about 16 years old.

In the early history of the subject most of the radium treatments consisted in applying to the lesions containers (usually glass tubes) with radium salts in them. Sometimes these tubes were inserted into the mass of the tumor itself. Soon, however, this crude method gave place to a more scientific technique. A number of scientists, a physicist, a chemist, a pathologist, a clinitian, etc., grouped themselves together under the leadership of Wickham and in 1905 began a thorough study of radium therapy. They invented an elaborate instrumentarium and devised several methods of treatment, among which the "cross-fire" and "filtration" methods may be mentioned. Radium therapy having attained some success, especially in the treatment of small superficial lesions, a number of individuals and institutions, both in Europe and America, undertook the systematic application of radium to a great variety of pathological conditions. Among these institutions the Radium Institute, of London, may be mentioned. This institute has several grams of radium at its disposal, and was the first actually to use large quantities of emanation as a substitute for radium in the treatment of tumors, it having been proved years before in Paris that the emanation of radium by itself and apart from the radium produces profound physiological changes. At Harvard, in the cancer commission's hospital, we have been using several methods I devised for applying the deposited activity of radium (radium, A. B. C.). Radium transforms itself into radium emanation, and the emanation in turn transforms itself into radium A. B. C. It is a well-known fact that the rays usually used in radium therapy come from radium A. B. C. and not from radium itself or its emanation. The first treatments by these methods were made by the author in collaboration with Dr. Greenough, Dr. Tyzzer, and Dr. Ordway in 1913. The methods have proved to be very flexible and it is possible by them to obtain very intense radiation over a sharply defined surface or throughout a given tumor mass.

The fundamental problem involved in treating a tumor with radium may be stated thus. Having a tumor of a certain size and shape, one must send through it a quantity of radiation sufficient to kill all the tumor cells with as little irritation of normal tissues as possible. The solution of this problem is largely a question of physical science. There are more than 30 known radioactive substances emitting in different degrees, one or more of four different kinds of rays, and one must choose a sufficient amount of the proper substance, place it in the right position in or near the tumor, and leave it there for a sufficient length of time. Evidently judgment as to quantitive relations enters as an important factor into the selection of the proper mode of procedure.

Some interesting principles underlie the methods of treatment mentioned above The "cross-fire" method is based on the geometry of radiation. The "filtration" method was devised for the purpose of cutting out those easily absorbed rays that would not penetrate far enough into the tissues. We know that the radium series of substances emit more than 64 different kinds of β rays and 14 different kinds of penetrating γ rays. These differ from each other enormously in penetrating power. The more easily absorbed kinds of the β rays are completely stopped by thin layers of tissue, whereas these same layers absorb only a very small fraction of the penetrating γ rays. Thus the amount of radiation absorbed by a given thickness of tissue is not at all proportional to the amount of radiation that enters it.

Usually radium treatments are given for lengths of time that vary in different cases from a few minutes to 60 or 70 hours. The relative value of the small dose for a long time and a large dose for a short time has not been very completely investigated. I propose in this paper to present some observations on the effects produced on carcinoma tissue by "prolonged radiation" with β and γ rays. By the terms "prolonged radiation" I mean radiation lasting continuously for a month or six weeks. Of course small quantities of the radioactive substances are used, which is a great advantage, considering the price of radium.

The technique of the treatments is as follows: A small quantity of radium emanation (from 3 to 10 millicuries) is extracted from the radium, purified, and compressed into a tiny glass tube (length 3–5 mm., diameter $\frac{1}{4}$ mm.). A brief description of the method of doing this that I have devised may not be out of place. The emanation is a chemically inert gas, and a millicurie is the quantity of emanation that is associated, or in equilibrium, with a milligram of radium element.

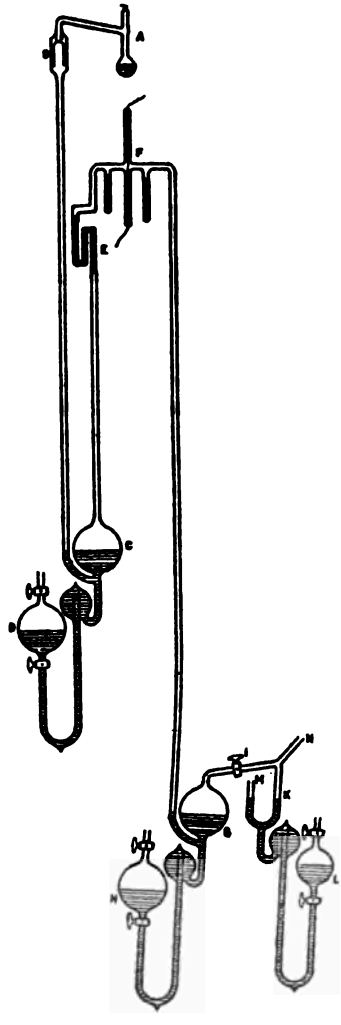
The general principles of the method of purification are those previously employed by Ramsay and Soddy, Rutherford, and Debierne, in some of their most important researches. The advantages of my method described below are: That the purification does not require liquid air; that a large number of millicuries of emanation can be purified and compressed into a small fraction of a cubic millimeter, in 10 or 15 minutes of time; that no emanation is lost except that due to its natural decay; and that the process may be repeated a great many times without renewing parts of the apparatus.

The drawing[1] represents the arrangement of the glass tubes and reservoirs. The bulb A contains the radium salt dissolved in water. Radium in solution continually decomposes the water into hydrogen and oxygen, and at the same time transforms itself into the emanation, which is set free. The total volume of the hydrogen and oxygen amounts to more than two hundred thousand times that of the emanation at the same pressure and temperature. In addition to the oxygen and hydrogen and emanation, a small quantity of helium appears (the volume of which is a few per cent greater than that of the emanation) and also traces of other gases, probably carbon dioxide and hydrocarbons coming from the decomposition of organic impurities, although the source of these traces of gas does not seem to be thoroughly understood. On account of its radioactive transformation, the exact proportion between the quantity of emanation and the gases with which it is mixed, depends upon the length of time the gases are allowed to accumulate. In the ordinary daily routine of our laboratory, however, the problem resolves itself into the extraction of 35 to 60 millicuries of emanation having a volume of 0.021–0.036 mm. at atmospheric pressure and ordinary temperature, from a mixture of gases, having a volume of 4.5 to 9 c.c. at the same temperature and pressure.

The mixture of gases collects in A and the tube B, and also, if the passage is open, in the reservoir C. Allowing the gases to collect in C apparently increases the efficiency, probably because the emanation defuses from the solution into a large volume more freely than into a small one. The tube B is considerably longer than 76 cm. so that air may be admitted into C, if desired, without its finding its way up

[1] See page 505.

to the radium solution. The trap at *B* protects against mercury spurting up into the radium solution, should some of the glass apparatus break. An ordinary water aspirator with suitable stopcocks controls the flow of mercury between the reservoirs *C* and *D*. On admitting the air into *D*, the mercury rises in *C*, pushing the mixture of gases through the mercury trap *E*, into tubes *F*. The mercury in the trap *E* holds back all but a very small quantity of the water vapor. The tubes *F* contain a copper wire slightly oxidized, phosphorpentoxide and potassium hydroxide. Although



represented in the figure in a vertical position, the copper wire really lies horizontal. It is wound on a quartz rod supported by feet, so that the wire does not touch the inner surface of the tube at any point. The diameter of the wire is 0.3 mm. and the length of the coil 25 c. m. When heated red hot by an electric current of 5–10 amperes it rapidly combines the oxygen and hydrogen, the phosphorpentoxide absorbing the water vapor formed. A small amount of copper oxide on the wire is required, because

the mixture of gases contains, at least at first, a quantity of hydrogen that exceeds by a few per cent the proportion required by the chemical formula for water. Some oxygen remains in the radium solution as hydrogen peroxide. The copper wire was heated for a long time to remove as much of the occluded gases as possible, and the phosphorpentoxide was distilled into its present position from a tube sealed on just below it, and afterwards removed; both of these processes taking place in vacuum. The potassium hydroxide is for the purpose of absorbing any carbon dioxide that may be present, or may be formed by the hot copper wire oxidizing hydrocarbon gases.

After the purification of the emanation the mercury in the reservoir *G* is drawn into *H*, the air being removed from *H* by the water aspirator, and the emanation and helium pass into *G*. The gases are then pushed up by the mercury through the stopcock *I* and into a capillary tube, which is sealed on at *N*. The volume of the helium being very small it is unnecessary to remove it. The length of the tube connecting *E* with *G* should be so great that air may be admitted into *G* without forcing the mercury up into *F*.

The stopcock *I* has a mercury seal and contains no stopcock grease. A few marks made with a lead pencil on the stopper allow it to turn freely. It will be noticed that the emanation passes through no stopcock except the one at *I*, and even this is unnecessary and has been added for convenience of manipulation only. The fact that stopcock grease and many other organic substances are decomposed by the rays from the emanation and give off gases is well known.

The system of tubes and bulbs *K*, *L*, *M* is for the purpose of removing the air from the other tubes and reservoirs, etc., by means of a pump attached at *M*. This must be done at the beginning, and after that no air enters the reservoirs except occasionally when it becomes necessary to renew the oxidized copper wire or the phosphorpentoxide, etc.

The apparatus in our laboratory has been in continuous daily use for more than two years. The bulb *A* contains over 220 milligrams of radium (element), and the total quantity of emanation purified per month amounts to slightly more than one curie of emanation, which is the quantity of emanation in equilibrium with one gram of radium (element).

After the emanation has been pushed up into the capillary tube at *N* suitable lengths of it containing the required amounts of emanations are sealed off by means of a tiny gas jet.

In making a treatment several of these tubes are inserted through a small trochar into the tumor or necrotic tissue and left there indefinitely. Great care must be taken in placing the tubes. They should not lie too near the normal tissues but, on the other hand, they must be so distributed that all parts of the tumor receive adequate radiation. I have seen carcinoma cells destroyed at a distance of 2 c. m. from one of these tubes, whereas normal epithelium may continue to live within much less than 1 c. m. of one. Several of the tubes properly placed produce an effective cross-fire.

As stated above, the emanation transforms itself into radium A. B. C. and the radium A. B. C. produces the rays that penetrate the tissues. Now the emanation gradually disappears. The law of decay is such that one-half a given quantity will have transformed itself and disappeared in 3.85 days. Thus at the end of four days about half of the emanation remains, at the end of eight days only one-fourth remains, and at the end of a month there is scarcely any left. If the case warrants it new tubes may be inserted at the end of one or two weeks so as to keep up a more uniform flow of β and γ rays.

The treatment produces surprisingly little irritation in surrounding healthy tissues. This was contrary to my expectations. In several cases tubes have been placed within 2 or 3 cm. of the eye without producing an effect beyond a slight increase in



June 7, 1915, case 1a.



May 2, 1916, case 1b.



July 7, 1915, case 2a.



November 27, 1916, case 2b.

the flow of tears. The side of the nose, too, was not burned, only a slight erythema appearing there. One patient claims to have been conscious of a sensation of light with the eyelids closed and in a dark room. This is a well-known phenomenon and is supposed to be due to a slight phosphorescence produced by the rays in some substance in the eyeball.

The fact that the rays have such a pronounced destructive effect in the immediate neighborhood of a tube and exert very little influence a short distance from it is due not only to the law according to which radiation from a point decreases as the square of the distance but also to the great absorbibility of the majority of the β rays. No effect can be produced by rays without absorption of energy, and it would seem in general advisable to use those rays a large fraction of the energy of which is absorbed by the tissues, rather than those rays which pass through without producing much change. This is contrary to the general practice of so-called deep radium therapy in which the easily absorbed rays are cut off by screens. In the method we are now discussing the deeper-lying tissues are reached by actually placing the source of the rays near them. The thinness of the walls of the glass tubes allows the easily absorbed rays to pass through into the tissues.

Some experimental evidence has been obtained in favor of the view that radiation has a greater effect on tissue cells during certain periods of their life history than at other times. If this is true in general, prolonged radiation will catch a larger proportion of the cells during their more vulnerable periods than radiation of short duration will.

Some details of the destruction of carcinomata and of subsequent tissue repair are given below.

The adjoined reproductions from untouched photographs represent the first three superficial carcinomata that have ever been treated by the prolonged radiation method. Each case is illustrated by a series of photographs showing the destruction of carcinoma tissue and the subsequent repair.

The following tables contain the data relative to the prolonged radiation treatments. In addition to these treatments steel tubes containing a few millicuries were occasionally applied for a short time (one-half to 2 hours) to portions of the lesions, which it was thought had not received sufficient irradiation. The greater part of the effect, however, was undoubtedly due to rays from the tubes inserted and left in position for several weeks.

Case I.—In April, 1914, the patient presented himself to the Huntington Hospital with a small tumor over the right malar bone that had appeared six weeks before. He received a mild radium treatment, but was advised to have the tumor excised. He went elsewhere, and some months later the operation was performed. Toward the end of May, 1915, however, he returned to our hospital with marked recurrence and received the following prolonged radiation treatments:

May 27 two tubes containing a total of 8.3 millicuries of emanation were inserted near the outer right-hand border of the lesion and left there.

June 2 two tubes containing a total of 6.3 millicuries of emanation were inserted, respectively, into the upper and lower borders of the lesion and left there.

June 7 the emanation tubes were still in position, but they could not be seen, as they lay below the surface of the necrotic tissue. No appreciable change had taken place since the patient returned to the hospital on May 27. (Case 1a.)

June 12 one tube containing 5.1 millicuries of emanation was inserted near the corner of the lesion below the inner canthus of the right eye and left there. From this time on a gradual but marked improvement took place. Epithelium gradually grew over the base of the hollow but never quite covered it. A small necrotic area still persisted on August 19. During September a marked recurrence took place, starting from the center of the lesion and spreading through into the mouth. It appears as if

the center had not received sufficiently intense radiation. I had thought that the cross-fire radiation received at the center from the tubes inserted around the borders would have been sufficient, but the facts do not seem to verify this. During October and November the lesion received a prolonged treatment somewhat more intense than the first. The hollow is now somewhat deeper, but no change in either direction has occurred during the last six weeks. It is interesting to note that although the right-hand side of the nose has been subjected for a long time to weak β and γ radiation, no ulceration has resulted. A slight erythema appeared, however, which does not show in the photograph. (Case 1b.)

Case 2.—The patient was referred to the Huntington Hospital on July 6, 1915, with multiple keratoses on his face and hands, some of which were of 10 years' standing. In several places they had definitely degenerated into carcinomata and had ulcerated; notably on the upper lobe of the left ear. All these lesions were treated, but only that on the left ear received prolonged radiation. Tubes containing emanation were inserted and left as follows. (Case 2a.)

July 7, one tube, 2.1 millicuries; July 14, two tubes, 7 millicuries; July 21, two tubes, 9.1 millicuries; July 28, two tubes, 15 millicuries.

Very little change appeared until July 28, and about this time the tumor began to diminish in size. The tumor continued to melt away until August 16. As the lesion did not seem to be improving much at this stage, August 24, two tubes containing a total quantity of 7.4 millicuries of emanation were inserted and left. After this treatment the ear swelled up to four or five times its natural size. The swelling, however, and the rest of the tumor gradually disappeared until only a small scab remained. A small piece of the edge of the lesion was excised, and Dr. Tyzzer found no evidence of carcinoma in it. Since this date the lesion has remained healed, as indicated by figure 2b.

Although some erythema appeared on the skin covering the side of the head, no ulceration occurred there, except where the tumor was actually attached.

Case 3.—The patient presented himself at the hospital on October 8, 1915, with an epidermoid carcinoma over and just below the right malar bone. This he said had developed from a small pimple, that had appeared eight years before.

Prolonged radiation treatment began several days later, and tubes containing emanation were inserted, and left as follows:

October 13, two tubes, 9.3 millicuries total dose, in the upper and lower borders of lesion, respectively.

October 27, three tubes, 10.1 millicuries total dose, one in the left-hand and two in the right-hand border.

November 3, two tubes, 4.4 millicuries total dose, in the upper and left hand borders, respectively.

Scarcely any effect had been produced up to October 27, at which time the photograph 3a was taken. There are five tubes in the borders of the lesion as represented in this picture. About this time the tumor began to disappear and by November 23 most of it had gone. The neighboring skin showed considerable erythema, but no ulceration has ever occurred beyond the edge of the original lesion, although some of the tubes were placed within a short distance of the normal tissue. Since November 23 the slow healing process has continued. Figure 3b represents the condition on March 10 and July 21, 1916, when the patient was last seen at the hospital. Examination of a small piece of tissue excised from the scar showed no evidence of carcinoma.

Every action that takes place in nature is not only qualitive, but also quantitive; and I have presented the foregoing data largely for the purpose of calling attention to the quantitive relations.

The quantities of emanation in the individual tubes varied from 1.1 millicuries to 7.5 millicuries, and at no time was a total quantity of more than 16 millicuries left



October 27, 1915, case 3a.



March 10, 1916, case 3b.

for a long period in a tumor. The tubes remained in position long enough to utilize the activity of the emanation during practically its entire life.

Unfortunately the space and time relations can not be accurately measured. The volumes of the tumors throughout which the rays destroyed tumor tissue may be estimated, however, as lying between 15 and 50 cubic centimeters. In the time relations we recognize three distinct periods, which may be roughly estimated (for the dosages given) as follows: (*a*) a latent period of 10 to 14 days, during which little apparent change takes place; (*b*) a destructive period of 3 to 4 weeks, during which the tumor tissue disappears as such, and (*c*) a period of repair, which may last for several months.

The word "specific" can not be applied strictly to radium rays. The rays however, have a certain "differential" effect on many kinds of tumor tissue, and the prolonged radiation method brings this out quite clearly. Some of the tubes mentioned above were placed within a few millimeters of normal tissue without producing a destructive reaction, and yet the rays from them destroyed carcinoma tissue at a distance of considerably over 1 centimeter.

It may not be superfluous to add that the prolonged radiation method offers no guarantee against recurrence.

We hope that the above described method may prove useful in treating internal malignant growths. Investigations in this field are in progress.

The CHAIRMAN. The papers by Dr. Wood and Dr. Duane are open for discussion.

Dr. EWING. I was extremely gratified to learn from Dr. Wood's closing remarks that he believed that in the course of a year or two methods would be offered to the clinician to enable him to treat cancer with radium, so I judge that he anticipates that eventually the agent will have some place in therapeutics. I think the doctor is perhaps not thoroughly familiar with the extent to which this agent has been used, nor with the results which at least careful observers are claiming for it. I have here an extract of 38 reprints, recent ones, on the therapeutic effects of radium from different localities all over the world. They cover 390 reported clinical cures of cancers, most of them of inoperable type: Fifteen of the tongue, 8 of the lip, 9 of the rectum, 17 of the prostate, 38 of the breast, 254 of the uterus, and 49 sarcomas, among which were 3 of the larynx, 5 of the oesophagus, and 3 of the thyroid. These are the reports of competent men.

Now, of course, the use of radium in cancer is like every other method which has been developed for the profession. It is simply the beginning of perfection; and radium is not a perfected product in the treatment of cancer to-day, but it is probably becoming so rapidly.

One should be very cautious about making any statement in a lay gathering as to the use of radium which might reach the newspapers. But at our meeting of the American Association for Cancer Research I do not think we ought to permit ourselves to be deceived as to its possibilities. We ought to realize that we expect to make progress in this matter; that we may not be getting to-day as good results as we may later; and on that point I wish to say that I disagree entirely

with Dr. Wood in his statement that to submit to radium treatment any operable case of cancer is malpractice. I can not agree with that. When one considers the result, for instance, as in the case Dr. Duane presented, of a small rodent ulcer of the face, and sees the result in a few weeks of the radium method, and then compares it with the method Dr. Duane used, I think one has every right to say that the use of this method is not malpractice. As a matter of fact, I think it is clearly demonstrated that the treatment of cancer by radium is a physical problem—that there is an energy in this substance which destroys cancer cells—and that if you get enough of radium applied in the right conditions you can destroy a cancer cell wherever it can be reached. I think, therefore, that the work Dr. Duane is doing in the physical control of the agent itself will reach the result which we are always hoping will be reached.

Dr. CLOWES. I was particularly impressed by Dr. Wood's experiments with radium, going through a series of generations; and, as I understand Dr. Wood, he appears to acquire a type of adaptation of the tissues to radium; that is to say, the tissues become more or less resistant, which is a matter of immense importance. In all our work with cancer, in the use of immune serum, chemicals, colloidal methods, etc., we have very frequently encountered conditions in which a tumor apparently would be temporarily relieved and then the same agent would under no circumstances produce a result again; and furthermore, we have every reason to believe that that condition can be transmitted from generation to generation. That is a matter of the greatest importance, because if that is the case, it means that whatever agents we employ in dealing with cancer—chemical, physical, or biological—should be used at the very beginning in the exact anatomic dose; otherwise, we make an adaptation of our tissues to a new environment and there is no longer response to any sort of treatment. I think that point is very important from a biological point of view, because biologists claim that all cells after a certain time revert to type and lose their specific adaptation to environment.

I believe to-day that the failure of ourselves and of other workers to reproduce some of our earlier immune experiments and some of our earlier chemical experiments are undoubtedly due to the same proposition, and I would point out that colloids can be adapted to the environment and that the surface tension can be changed and adapted to environment. It is possible that this whole matter may be a matter of surface tension.

Dr. LAMBERT. Just a word about the paper and the remarks of Dr. Ewing. Although this is a meeting of the American Association for Cancer Research, I fear that a repetition of some of the statements in the newspapers is capable of a good deal of harm. I would like to emphasize, therefore, one thing in Dr. Duane's paper, e. g., that these

lesions of the face were probably the rodent ulcer type of a very low grade of malignancy which do not metastasize—many have been cured by X-ray treatment—and I do not know but that Dr. Duane suggested operative procedures.

Dr. DUANE. It was done.

Dr. LAMBERT. Can you vouch for the type of operation that was done?

Dr. DUANE. It was done in the Boston City Hospital.

Dr. LAMBERT. It seems to me in regard to the work that is being carried on by Dr. Loeb and others who are trying to educate the public in regard to these matters that it would be unfortunate if statements referring to rather remarkable cures with radium treatment should go out from a meeting of this sort.

Dr. WOOD. I seem to have misled Dr. Ewing in my views. I have not changed my opinion that the radium treatment of an operable tumor is at the present time not justifiable and is not good practice. I am also not unaware of the reports in the literature; for instance, there are three cases of carcinoma of the esophagus reported cured. I autopsied one of them. The other two I know died within a few weeks after the treatment was made. The amount of radium in the tube was probably about 2 milligrams of the element. Further comment, you see, on that kind of cure is not necessary. We all know, for instance, the cases which are heralded widely in the papers. Take, for example, the case of famous old Uncle John, who after a few months has had his picture shown as a great cure—he died some time ago with metastasis of the liver. As Dr. Lambert explained, there are many factors which make a case operable or not, and that is what I mean when I speak of operable cures. A man of 80 who has a tumor of the eyelid which would destroy his eye and has perhaps a year or two to live, I do not consider a good operable risk, and would, of course, subject him to radium. But the later recurrences which we see following radium cures are very extraordinary; recurrences which happen after six months, one year, two years, three years—and I saw one of eight years the other day, after X-ray treatment of epithelioma of the lip, a recurrence in the glands of the neck which was the size of a melon. Unfortunately, many of the cases reported were not microscopically examined; unfortunately, many of those that were reported as cures have since died; and most of the cures are tumors that are relatively benign, benign tumors that are removable by curette. The treatment of epithelioma of the face, I think, is justifiable by radium, but if I had one I should prefer to have it cut off.

Dr. WILLIAM DUANE. I would also like to call attention to the fact that I never used the word "cure." I never use the word "cure" in speaking of a malignant tumor. In regard to the lip cancer, as

a matter of practice we always operate on them; and in one or two cases where the patients refused operation, we have refused to treat them with radium, because Dr. Greenough, who is our surgeon, feels that those lip cancers should be operated on.

CHAIRMAN. This concludes the discussion on these papers and we will now take up the paper of Dr. Ewing on "Pathological aspects of some problems of experimental research."

PATHOLOGICAL ASPECTS OF SOME PROBLEMS OF EXPERIMENTAL CANCER RESEARCH.

By JAMES EWING,

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Although the great possibilities presented by the study of transmissible tumors of lower animals were fully revealed in 1894 by the systematic observations of Morau, it was not until 1901–2 that the work of Loeb in America and Jensen in Denmark attracted universal attention to this field. Especially in the last decade a great number of observations from a host of workers have produced a body of new data which is of first importance in oncology. From this extensive field it is my purpose to select for discussion certain problems which are of special interest to the general pathologist and to attempt to evaluate the new contributions by the old and established pathological criteria.

Prominent among the questions raised by the study of transmissible tumors of lower animals is whether these processes are genuine neoplasms. Considering that Virchow once said that no one even under torture could state exactly what a tumor is, this question must appear somewhat academic. Yet to the older pathologists, thoroughly saturated with the conviction that a neoplasm is viable only in its host, the demonstration of successful transfer to a new host naturally raised a lively scepticism. Transmissibility implied to them infectiousness and a granulomatous nature; the transplantable tumors must be shown to grow solely from the transplanted cells, after the manner of metastatic tumors, they must exhibit infiltrative growth, and produce metastases; the striking morphological resemblance to tumors was not universally regarded as decisive evidence. All these essential attributes of true malignant tumors have now been demonstrated for many of the transplantable growths in lower animals.

Personally I consider the morphology alone as a sufficient guaranty of the neoplastic nature of many of these tumors. Doubts of its significance seem to result from a somewhat narrow conception of the very variable morphology of the cancer process, and similar doubts have arisen regarding the cancerous nature of certain human tumors of peculiar character. Thus Borst discusses the question whether primary liver cell carcinoma is a true carcinoma because the infiltrating cells are mechanically forced into the hepatic capillaries and do not actively grow into them as do some tumor cells. Yet it seems somewhat arbitrary to demand that hepatic carcinomas should behave exactly as do mammary carcinomas. The hepatic carcinomas have many peculiarities of their own, but all the essential characters of malignant tumors. Similar reservations may be made regarding carcinomas of the thyroid, stomach, adrenal, and other organs, in which morphological details are not cut to exactly the same pattern. Moreover, cancer morphology does not always appear at its full development, but is progressively unfolding its potentialities.

Analyis of the structure of human cancer reveals the following features, any one of which may dominate the picture or any combination of which may be exhibited.

1. Hyperplasia, surpassing that observed in other conditions occurring in the same organ. A sliding scale is here necessary owing to the great variations in the degree of hyperplasia resulting from inflammatory and functional changes in the different organs.

2. Atypical qualities of the cells. This feature is universally recognized as perhaps the most significant criterion of a malignant process, and when sufficiently pronounced may stamp the process as malignant in the absence of other changes (early carcinoma of the larynx).

3. Loss of polarity. The regular alignment of cells in relation to one another and to basement membranes may early be lost in adeno-carcinomas, and is completely destroyed in diffuse carcinomas.

4. Desmoplastic properties. The capacity to excite the growth of connective tissue is very prominent in most carcinomas, but entirely lacking in others. Mammary fibrocarcinoma and embryonal carcinoma in children represent the two extremes.

5. Infiltrative growth is a late property of most carcinomas and the time of its appearance depends much on the accidents of position.

6. Metastases. As an objective sign the occurrence of secondary tumors is most convincing evidence of a lawless growth, but in benign metastasizing struma they occur early, in an otherwise innocent tumor, and in some types of malignant hepatoma they never develop.

Judged by these main criteria, the tumors of lower animals take their places as malignant neoplasms, with certain peculiarities which are impressed upon them by their species.

Metastases were observed and experimentally produced by Morau, and Murray found them in 50 per cent of his mouse tumors. Their relative infrequency as compared with those of human tumors may be referred largely to the short duration, and the peculiarities of the circulation in small animals. Infiltrative growth is frequently observed under suitable conditions, especially when the tumor meets resisting structures. The degree of cellular hyperplasia may be so great that the tumor outweighs the host, and in general it probably attains a larger relative volume than in human tumors. The atypical qualities of the cells are almost constantly pronounced, but while this feature has been emphasized by some, I have gained the impression that the variations in tumor morphology in lower animals are less violent and less extensive than in the human subject. Extensive overgrowth of connective tissue is also much less notable in the small animals for reasons which are not entirely clear.

I have extended this analysis to some length because the study of lower animal tumors has forced the pathologist to relax to some extent certain rigid notions regarding what a tumor may do and how it may look.

The comparative studies have not, however, revealed any striking variations or new morphological properties beyond those occasionally exhibited by human tumors. The same fixity of form and clinical behavior reappear in the different examples of the same type of tumor, and this morphology is usually maintained throughout many generations of transplants. The structure may vary in different portions of the same tumor, and metastases may be more or less atypical than the original growth.

There is one important phenomenon exhibited by lower animal tumors, however, which is at variance with the rules deduced from human oncology. Certain transplanted tumors of mice and rats are said to excite a neoplastic process in the stroma of the host so that in the course of transplantation a stromaborn sarcoma may arise and even outgrow and eventually eliminate the original carcinoma. This phenomenon was first observed by Ehrlich and Apolant in the tenth generation of an adenocarcinoma of the mouse, and has been reported in both rats and mice by Loeb,

Lewin, Bashford, Haaland, Russell, and others. The change appears to occur rather suddenly in the eighth to tenth or later generations. Russell fixed the usual period at the fifty-fifth to sixtieth day of propagation and states that it is independent of the number of transfers.

When once established it is usually progressive and both tumors persist together, or separate strains of sarcoma and carcinoma are obtained in subsequent transplants. The rate of growth of the mixed tumors is usually increased and the sarcoma is usually more active than the carcinoma, and is more frequently encountered in metastases (Haaland, Clunet).

The idea that the original growths were mixed tumors was abandoned for lack of any evidence. It is generally concluded that the sarcoma represents a neoplastic transformation of the stroma of the host caused by a stimulation of cells by the tumor epithelium. Both Haaland and Russell describe in detail the appearance of foci of overcellular stroma located in the center of carcinoma nodules, the increase in mitotic figures in the stroma cells, the survival of these altered cells in grafts, and their rapid increase until they overgrow the epithelial elements.

There is no counterpart in human pathology for this remarkable process. In no case has the stroma of a human tumor during vicissitudes of prolonged growth, inflammatory reaction from infection, recurrence after operation, or spontaneous metastases, taken on a neoplastic growth. It is true that very notable grades of reactive hyperplasia may be excited by the invasion of cancer cells. The most remarkable is probably seen in the bone metastases of prostatic carcinoma (v. Recklinghausen). Here there is very extensive overgrowth of bone following carcinomatous invasion, and histological study does not always succeed in separating tumor cells from multiplying osteoblasts in the new tissue. The process has been regarded by some as possibly sarcomatous; and secondary osteosarcomatous metastases are said to occur in the lung (Schmorl, Fischer-Defoy, Axhausen). Yet it is not clear that the osteoblasts take on true neoplastic properties, and the pulmonary nodules are generally regarded as osteoplastic carcinoma.

It is perhaps unreasonable to expect that there should be a human parallel, for human tumors do not experience quite the same insults as transplanted tumors receive. Yet it is a well established rule that the stroma never participates in the lawless growth of cancer cells except in mixed tumors, and it is distinctly anomalous that no trace of this sarcomatous transformation appears in man, when it is relatively common in mice. Under these circumstances it may reasonably be demanded that entirely demonstrative evidence should be furnished before its occurrence in mice can be accepted. Not having actively engaged in this study I am not in a position to deny the claim of the very competent investigators on whose evidence the interpretation rests, but it may be permissible to point out some of the difficulties in the way of accepting their interpretation that the stroma of mouse cancer becomes sarcomatous.

Human carcinoma never exhibits a sarcomatous transformation of its stroma, but its polyhedral cells frequently lose all their epithelial characters and grow in spindle form. Epithelial tumors may from their inception appear like spindle cell sarcoma, as in the spindle cell basal-cell carcinomas of Krompecher, in spindle cell carcinoma of the thyroid, and in melanoma. It is becoming more and more apparent that many so-called sarcomas of the organs are in reality spindle cell carcinomas. Or the change to spindle cells may occur in one portion of a typical carcinoma as is frequently seen in tumors of the thyroid gland, and liver; or spindle epithelium may regularly appear with columnar, as in glandular adamantinoma. This tumor is notorious for its remarkable changes of cell form. In recurrences after operation on typical carcinomas, one frequently encounters pure spindle cell growths. I have traced an adamantinoma recurring after four operations, through the structures of adult acanthoma, plexiform epithelioma without squamous cells, spindle cell sarcoma, and finally round cell

sarcoma. Recently I have found spindle cell perivascular sarcoma in a uterus, removed shortly after curettage, revealing typical adenoma.

Spindle tumor cells are so common in carcinoma that their occurrence in any carcinoma is very strong presumptive evidence that they are altered epithelium.

The intrinsic evidence relating to the transformation of the stroma is not entirely satisfactory. The change is sudden and coincident with an increased rate of growth of the tumor, as is the case with human tumors assuming the spindle cell form. A new tumor process, affecting the stroma, might be expected to develop more gradually. The new tumor process seems to outstrip and may eliminate the old. This observation, that an original carcinoma should yield its powers to the stroma cells and itself retire from the scene, seems highly paradoxical. The reverse process, viz., the elimination of spindle cells in the course of transplantation of a carcinoma has been observed by Apolant, but here the spindle cells were interpreted as altered epithelium. The fact reported by Haaland, that the carcinomatous element in the mixed tumor may be eliminated by heating to 44° C., is a suspicious circumstance and indicates that the spindle cells are merely the more resistant as well as the more rapidly growing form of epithelium.

The crucial evidence is that presented by observations tracing the actual transformation of stroma cells into the spindle cell sarcoma. Not all authors have been able to convince themselves that the stroma really gives origin to the sarcoma but Russell and Haaland have traced this origin in detail. Haaland pictures peculiar halos o. large pale cells surrounding epithelial groups. They are intermediate in form between stroma and tumor cells but Haaland derives them from the former. Yet the interpretation of transitional pictures is notoriously hazardous and few observers have been willing to trust it in this connection. Orth thought that Lewin's sarcoma represented granulation tissue. Through the kindness of Woglom, I have examined two cases purporting to show the sarcomatous transformation of stroma cells, but have been forced to draw from these sections the opposite conclusion, namely that the spindle, cells are derivatives of the epithelium. In view of all these difficulties it may be urged that further evidence is required before the sarcomatous transformation of mouse carcinoma can be accepted as proven. The writer would not deny its occurrence but merely asks for more evidence.

The experimental studies have not succeeded in defining what constitutes a tumor. They have shown indeed that perhaps the most essential property of tumor cells is the capacity for unlimited growth in a wide range of environments. A vast number of experiments in the transfer of normal or proliferating cells of embryonal or adult type has shown that these cells may multiply for a short period but soon differentiate and become quiescent, or atrophy and disappear. Transplanted tumor cells, however, continue to proliferate beyond the life-time of the host from which they were derived.

Yet just this conspicuous tumor character is exhibited in a notable degree by two diseases the exact nature of which has not been fully determined—the so-called infectious lymphosarcoma of dogs, and Rous' chicken sarcoma.

The infectious lymphosarcoma of dogs is transferred by coitus and also by other methods of contact. It affects primarily the genital organs, skin, kidneys, and some other organs, and produces bulky primary tumors as well as milary or massive metastases. The gross anatomy is typical of a malignant neoplasm, and the microscopical structure also is that of an extremely active, atypical, infiltrative, malignant tumor. It probably arises from the reticulum cell of the lymph node. No microorganisms are demonstrable in unulcerated tumors. Transplantation is successful only under the same conditions as govern the transfer of mouse tumors, i. e., the inoculation of living cells into closely related animals. Doubts regarding its true neoplastic nature arise from its evident relation to the lymphocytomas. Furthermore, it must be admitted that at some point in the history of its development a parasite may enter, though there

is no evidence that a parasite persists throughout the disease. Bashford concluded that the tumor grafts grew in part at least from the host's cells like a granuloma. In serial transplants studied by Beebe and the writer it grew exclusively from the transferred cells. Bashford, on examining these sections, admitted that they differed from his own, and I am forced to conclude that he was dealing with infected material or that some other factor caused unnecessary inflammatory reaction about the grafts.

v. Dungern claims to have dealt the "coup de grace" to this tumor by showing, through the absence of agglutinins for dog's corpuscles, that the tumors lose their dog protein when transferred to foxes and accumulate only fox protein. His hare sarcoma, which had likewise certain granulomatous features, preserved its hare protein while growing in rabbits. I must decline to accept v. Dungern's conclusions, based as they are on such evidence as agglutination and hemolysis. The tumor can be seen to grow from the transplanted cells, and in comparison with such direct evidence the significance of antibodies for a specific protein is of quite subordinate value. Moreover it appears reasonable that a few dog tumor cells multiplying many thousand times in fox tissue should rapidly acquire the fox stamp. Beebe has shown that mammary carcinoma growing in lymph nodes acquires the nucleohiston of lymph nodes which is entirely missing in primary tumors of the breast.

I think, therefore, that the lymphosarcoma of dogs may safely be regarded as a disease sui generis, but essentially neoplastic. It may be complicated by a parasite but the existence of this complication is not proven. Exactly the same uncertainties surround the origin and nature of human lymphosarcoma.

Rous's series of chicken sarcomas is one of the most interesting and obscure developments of experimental cancer research.

On morphology, one would accept his original tumor as a neoplasm. It presents excessive hyperplasia so far as may be judged by available standards. The atypical qualities of the cells are pronounced. There is infiltrative growth and metastases are ubiquitous. It was at first transferred with considerable difficulty and only to the same strain of chickens, but its viability gradually increased. Yet it violates the central criterion of tumor growth by being transmissible by means of tumor filtrate passed through a Berkfeld filter (No. 5 medium). The active agent will not, however, pass a Chamberland bougie F. Tumor tissue dried for some months remains active, but the resulting tumors are feeble. Exposure to 55° C. inactivates the agent. Cultures are negative.

On these data one must either discard the process from the group of neoplasms or alter the experimental criteria. The latter course seems the only logical choice.

In attempting to analyze the significance of this tumor we are handicapped because the principles of avian pathology are not well understood. One must hesitate to apply the standards of human pathology to the tissue reactions of the chicken. Exudative inflammation, functional and inflammatory overgrowth, metaplasia, etc., may follow somewhat different laws or standards in such widely separated species. Hence one may be in error in too closely identifying this chicken sarcoma with sarcomas in other animals. It may be an infectious granuloma with neoplastic morphology. But I do not think that either the granulomatous or the infectious nature is probable. The only infectious agent meeting the requirements would be an extremely labile protozoon, of the actual presence of which there is no tangible evidence. It has been suggested as a last resort that fragments of cell nuclei capable of reproducing the cells may pass through a Berkfeld filter. While the data are still inadequate to force any conclusion, I have received the impression that Rous's sarcoma is a genuine neoplasm, occurring only in the chicken, and that the transmissible virus is of chemical, and possibly of ferment nature. The extensive series of transplants has probably intensified the action of any such chemical agent present in the original tumor, so that effects are now being produced with this tumor which were not possible with the spontaneous growth and which probably have no counterpart in any other process spontaneously

occurring in nature. At any rate, the principles deduced from this process must for the present be appiled to this disease and to no other.

There are, however, some indications that chemical agents such as may be active in the chicken sarcoma, are also of influence in some human tumors. While many tumors, after their area of origin is defined, grow exclusively from their own resources, others grow by progressive inclusion of previously normal cells in the tumor sources. This principle comes to light in many different circumstances and may be employed to account for diffusely spreading or multiple tumors of serous, mucous, or cutaneous surfaces, and in systemic tumors of lymph nodes. In a lesser degree, it may account for collateral hyperplasia about the edges of some tumors. Paget's disease covering much of the chest and trunk would be explained thereby, and the pigment of melanoma is said to have excited the neoplastic proliferation of liver cells about hepatic metastases. So one may conceive that in the chicken tumor a chemical agent may exist which is remarkably effective in inducing neoplastic hyperplasia, and that either this agent alone or the cells that contain it may give rise to the tumor. It may here be recalled that the filtrate is much less effective than are the living tumor cells. Perhaps, also, chicken tissues are more responsive to such agents than are other animal cells.

It would be interesting to know if carcinoma in the chicken, of which Ehrenreich has described several, is also transmissible by means of its filtrate.

In determining the effects of changes in the soil upon the growth of the tumor, experimental studies have yielded results of much practical value. Spontaneous variations in the growth of tumors are quite as well established clinically as in the experimental field, but the latter seems to have revelaed some of the reasons. Racial differences in susceptibility have been practically identified with changes in the diet. The importance of carbohydrates in the nutrition of tumors has long been recognized among clinical writers and has been extensively discussed by Brault, Keating-Hart, and many others. The varying glycogen content of different human tumors suggests the caution that all tumors may not be especially dependent upon this class of foodstuff, and the complexities of carbohydrate metabolism indicate that it may be difficult to secure satisfactory experimental evidence in the field of tumor diets. Nevertheless it appears that rats may be made refractory to the Buffalo sarcoma by a previous course of carbohydrate-free diet, that the course of this tumor once established is retarded by such diet, whereas it is accelerated by butyrates among the fats. Benedict saw the complete regression of large sarcomas in rats rendered completely diabetic by phloridzin. By substituting foods rich in lime, Sweet, Corson-White and Saxon rendered rats markedly insusceptible to sarcoma, and saw much acceleration in growth on return to normal diet. Contrary observations show that all tumors do not react to dietary changes, but the important feature of this work consists in the demonstration that the subject is susceptible of experimental study and opens up one of the most attractive fields in experimental cancer research.

Age is found to have no definite influence on the susceptibility of tumor grafts. Both young and old animals have proven suitable for experimental propagation, although most workers prefer quite young subjects. This rule, which could hardly have been established except by experimental studies, has an important bearing on our conceptions of the relation of age to tumor incidence. Cancer has been held to be a disease of old age and yet young animals are the better soil for growing tumor cells. Hence it is not constitutional susceptibility but the effective action of inciting factors which belong to age. The problem of the inception of cancer is quite apart from the problem of its continuous growth. Experimental studies have had little concern with the histogenesis of tumors and only to a slight extent with their general etiology. In the transplantable tumors these important questions have suffered some neglect, but work in this field has been of great value in defining the influence of age, and separating the questions of inception from that of later growth of tumors.

Immunity: Although Lauder Brunton once said that immunity will eventually be found to be a function of the liver, the serologist will doubtless claim exclusive rights in this field. The pathologist may gladly yield this territory, pointing out that serology has signally failed to produce satisfactory evidence regarding the nature of resistance to tumor growth.

Animals in which a tumor has spontaneously regressed are often actively resistant to further implantation, but the resisting factors can rarely, if ever, be transferred to susceptible animals and specific antagonistic factors in the blood serum have not been satisfactorily demonstrated. On the contrary, it is rather clearly apparent that immunity to tumors is histioid and cellular and reveals itself in the reactive growth of connective tissue, phagocytosis, and lymphocytic attack on the tumor cells. A sufficient stroma reaction has been emphasized by many as the essential element in successful implantation, but abortive grafts are often found sharply inclosed in alien connective tissue. Phagocytosis is very frequently observed about grafts implanted in insusceptible animals, and many types of cells participate in this process.

Lymphocytosis and lymphocytic invasion are prominent in the reaction against grafts in resistant animals and about regressing tumors. There have been numerous observations pointing to the importance of lymphocytes, large and small, in the local and general reaction to tumor growth. Recently Murphy has shown that mouse tumors may grow in chicken embryos until the time when the production of lymphocytes becomes established, that this time may be shortened by implanting spleen tissue in the embryo, and that tumors may grow in alien species whose lymphocytogenic function is paralyzed by the X-ray.

Most of these observations on the mechanism of tumor immunity must be valued as confirming conclusions previously drawn from human pathology. Schmidt has shown that vagrant tumor cells are not destroyed in the circulating blood, but are lodged in capillaries, coated with fibrin, inclosed by endothelial cells, and reduced to fibrous nodules. It is highly probable that many tumor cells are destroyed in the lymph nodes which drain tumor areas. The function of lymphocytes in limiting tumor growth is extensively illustrated in human material. In many instances they form the chief barrier against the initial downward invasion of epidermoid carcinoma. In many mammary carcinomas one may see islands of tumor cells in process of destruction by lymphocytes, and polyblasts figure prominently in the active fibrosis which incarcerates many tumor cells. It is a well founded principle of pathology that degenerating or alien tissue cells are removed by phagocytosis. Reactive fibrosis limits the growth of many tumors more often in man than in lower animals, and may be interpreted as a form of cicatrcial healing. It may reach very extensive proportions; thus, I have seen nearly the whole liver transformed into scar tissue in which were very scanty remnants of an original metastatic carcinoma. Lymphocytic activity and extensive fibrosis are features that belong to the so-called clinically resistant cases, and are generally wanting in the more rapidly progressing carcinomas. These processes seem to be particularly prominent in very old subjects in whom carcinoma is of slow progress and often takes a scirrhous form. Back of these well known histological signs of the mechanism of immunity are doubtless submerged constitutional and local influences, in the elucidation of which tumor serology doubtless faces a significant future.

On the therapeutic side experimental cancer research still presents itself practically empty handed. The exclusive and quite energetic pursuit of the principles of serum immunity has accomplished practically nothing except to show that the malignant tumor process can probably not be controlled by investigations along the lines which have proven effective in bacterial diseases. Vaccination by means of tumor derivatives has been practiced on an enormous scale all over the world and has failed to justify itself. It has had some paradoxical success, but has probably done more harm than good. No one has been able to improve upon Vidal's feeble showing for anticancer sera. Chemotherapy has never had any tangible basis in the

tumor field, and from Weil's review it would seem to have even less claim to serious notice than has vaccination. Under these circumstances I venture to raise the question whether it is not time to abandon this unprofitable territory and seek for help in entirely different directions. It may be that artificial alterations in the course of metabolic processes in the body, as suggested by recent dietary studies, may prove capable of influencing favorably the course of some malignant tumors. I freely confess the hope that the vegetable kingdom may be found to contain some agent that will specifically affect the cells of some tumors. It is the genius of vegetable products specifically and powerfully to affect different organs, tissues, and functions of the animal body, as exhibited by digitalis, strychnine, morphine, etc. Why should not some vegetable agent attack the delicately balanced nutrition of tumor cells? It would be extremely disconcerting, and even mortifying, if some vegetable alkaloid or glucoside were found to do more for cancer than all the theories of serum immunity; but the demonstration, if made, would have to be accepted.

At present the only laurels in cancer therapy are being carried off by physical agents, X ray, and radium, and it seems to be only the difficulties of accessibility and dosage which stand in the way of the successful application of these agents to all localized and some generalized tumors. Cancer research should note that progress in the development of the X ray is almost exclusively in the hands of elaborately equipped and farsighted business corporations, from whom one department of medicine receives orders when and how to proceed. This situation is not flattering to our dignity. With radium the situation is somewhat different, since the study of the physics and therapeutics of radium rests with Government organizations, universities, and private institutions endowed with a supply of this precious metal. It is not too much to hope that when the early stages of cancer are recognized as a proper field for the use of X ray and radium, as has already occurred in the opinion of some competent authorities, much of the present fear of the disease, especially of the most deplorable post-operative recurrences, will be removed. In such an event some of the present problems of cancer research will retain only an academic interest.

In the department of special etiology experimental cancer research has secured some of its most significant results.

The chicken sarcomas are most suggestive from the point of view of their probable etiology and pathogenesis. Although there may be nothing like them in human pathology, they stand as a specific pathological entity and raise interesting questions regarding the etiology of other tumors. Borrel's consistent pursuit of animal parasites in tumors has enabled him and others to uncover the main factors in the causation of several tumors of lower animals; and it is not impossible, although as yet unproved, that they may have counterparts in man. When Fibiger discovered a nematode worm in the gastric carcinoma of rats, and by a brilliant analysis identified and located this parasite in nature and reproduced the disease experimentally, he established the existence of another specific disease of neoplastic character.

These contributions seem to me to point to the necessity of regarding all forms of neoplasms as specific diseases, connected only by the fact that they are neoplastic in greater or less degree, but differing in their etiology, clinical course, and therapeutic possibilities. In the same way tuberculosis and bubonic plague are infectious diseases of inflammatory nature, but they are quite as closely related as Fibiger's gastric carcinoma of rats and pipe smokers' cancer of the lip. The habit of regarding cancer as a protean disease of uniform significance may well be abandoned in the interests of progress. When cancer research properly occupies itself in the study of the distinctive features of different cases of malignant disease, especially when it abandons the idea of a universal cure for cancer, it will be in accord with sound pathological sense. It will then not be necessary to talk wisely to the public about the obscurities of cancer etiology or speculate about why cells grow lawlessly. Concerning the ultimate nature of neoplastic overgrowth we shall never have more than a descriptive knowledge.

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The CHAIRMAN. There are many points in this paper I would like to have discussed, but I think the hour is late and I must now call on Dr. Coca.

SERO-DIAGNOSTIC METHODS IN CANCER—REACTIONS OF FREUND AND OF V. DUNGERN.

By A. F. COCA,

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I have prepared no special paper, because the field of sero-diagnosis of cancer is the most unsatisfactory in cancer research, the most interesting and peculiar fact in regard to this field being that there are so many assumed sero-diagnostic methods published, evidence collected, and then entirely neglected. I would like to confine myself to an account of my experiences with the Freund reaction and the complement fixation reaction of Von Dungern.

About two years ago, thanks to the generosity of the trustees of the Huntington Fund, I was permitted to visit the laboratories of those two men and to study the results of these reactions, which they were perfecting. Freund's reaction was based upon the proposition that normal serum destroys cancer cells, whereas cancer serum is not able

to do this. The reaction is not only of clinical interest, but touches on the question of etiology, and it is this aspect of the subject that interested me most, because, after all, it is not strange that serum should not destroy cancer cells. The interesting thing is that it should do it at all. The reaction is performed with an emulsion of cancer cells, best taken from the liver at postmortem. The emulsion is prepared by squeezing the tissues through a wide-meshed towel into a solution of acid sodium phosphate, in which the tissue is left overnight to prevent agglutination of the cells; by centrifugization and washing the larger clumps of cells and cell débris are removed, and the isolated cells are deposited, so that at the end an emulsion is obtained in which the cells can be easily counted. In the laboratory of Freund there were eight such emulsions. These were preserved, with the addition of 1 per cent sodium fluoride, in the ice box. Three of the emulsions proved to be satisfactory for counting purposes, and in the experiments with normal human serum a solution was obtained of the cells in the way described by Freund. The cells are counted. There should not be more than 20 cells in 16 small squares of the blood-counting apparatus, and after incubation for 24 hours this should be reduced to 50 per cent. Sodium fluoride should be added to the mixture of the cell emulsion and the serum in order to prevent bacterial growth. In most of the succeeding experiments, however, in the same laboratory and using the same solutions and reagents, no solution of the cells could be obtained.

I used rabbit serum, horse serum, and normal human serum, all fresh, and in very many series of experiments; no further solution could be obtained, excepting in one single instance. I found that in the first place the sodium fluoride did not prevent the growth of bacteria at 37° C. Freund himself said that he had not investigated this. He did not know whether it was actually antiseptic or not. He said that he was using a 10 per cent solution of sodium chloride, whereas that substance is saturated at less than 5 per cent. In his publications he gives this percentage. I have tried other preservatives, notably boric acid and borax, in a mixture and have found that this is more successful in reducing the growth of bacteria. In fact, it can be used in preservation of blood for the usual purposes of complement fixation, but applied to tumor cells it is not useful, because tumor cells are agglutinated in it.

In many subsequent experiments, both in Hamburg and in America, all evidences of a dissolving influence of normal serum on cancer cells have been lacking.

Von Dungern's reaction is one that depends upon the usual technique of complement fixation. He got his idea, practically, from the published experiences of Ascoli and Izar in the use of the meiostagmine reaction, and his antigen was originally an alcoholic extract of tumor. He did not claim to have found a specific reaction in the sense that there were specific antibodies to the antigen, nor did he think that the reaction was an organ-specific one, in the broader sense—but he did think, and I believe he still thinks, that the substances producing the reaction were the result of an infection by a parasite which may under favorable circumstances result in the formation of a tumor. He conceives that the parasite is present in the blood of individuals long before the tumor has appeared. This experiment is made with an antigen in which the lipoids were isolated. In the later experiments of Von Dungern, instead of the extract of the tumor he used an extract of blood corpuscles. In one experiment I found that the blood lipoids used with the urine of cancer patients produced a reaction. The same substance used as an antigen combined with urine of syphilitic patients did not produce the reaction. There was a distinct fixation which seemed to be specific. The urine was not used in its crude condition, but an alcoholic precipitate was taken and dialyzed and brought up to a certain proportional volume in each case, and that was used in place of the patient's serum.

In many experiments since then, both in von Dungern's laboratory and here, no such reactions have been obtained. In fact, during the time that I was in von Dungern's laboratory his laborant was not able to produce a reaction. The reactions at that time were being carried out by an assistant as had been the case for sometime

previously and von Dungern had not been controlling the test, but an examination of them showed that they were not being carried out according to the usual principles of the complement fixation test. I have spoken with other men who have tried the reaction, among them, Sachs, in Ehrlich's laboratory, and these men have failed to obtain anything like the results reported by von Dungern. The confirmatory work has been done chiefly in von Dungern's laboratory. One of those who obtained confirmatory results in his laboratory, Halpern, has not been able to use the test at all since he has been working independently. There seems to be, as Sachs expresses it, an uncontrollable factor in the technic of the test that makes it not valuable for clinical use.

The CHAIRMAN. Is there any discussion of Dr. Coca's paper?

Dr. BRONFENBRENNER. I would just like to add one word in connection with the paper by Dr. Clowes, i. e., it would be very interesting if it were possible sometimes to prove that in tuberculosis and cancer the difficulty of serum reaction is due to excess of calcium, which interferes with the extent of the reaction.

The CHAIRMAN. I will now state that the paper of Dr. Bosco is to be read by title.

TERATOMA DE LA REGIÓN DEL TUBER CINEREUM.

Por GUILLERMO A. BOSCO,

Adscripto a la Cátedra de Clínica Propedéutica, Buenos Aires, Argentina.

Los casos clínicos, como el presente, son comunes, pero la naturaleza anátomo-patológica del mal es de las más raras. Esta es la causa que nos anima a publicar la siguiente observación y desde ya podrá suponerse el carácter de la misma. Revisando la historia anátomo-patológica de los tumores cerebrales, sólo hemos encontrado seis casos semejantes al presente, de los cuales ninguno corresponde a autores de nuestro país. Creemos, salvo mejor información, que el teratoma del tuber cinereum, objeto de este trabajo, es el primero que se describe en la Argentina. El encéfalo no es asiento común del teratoma; su proporción es mínima si la comparamos con el número de los que se desarrollan en sus regiones de predilección. La razón de ello se encuentra en la embriología, en la forma como se organizan los diversos segmentos de nuestro organismo, y que no recordamos para no alejarnos demasiado del propósito que nos hemos propuesto. Más llamativo es pensar en la causa que da lugar a la producción de estos tumores que, como se sabe, son embriológicos. Sería difícil imaginar algo nuevo, después de todo aquéllo que se ha expresado al respecto. Comparando las distintas opiniones reinantes, una sola queda en pie y es aquélla que los considera como una defectuosidad formativa, una reviviscencia desviada y monstruosa de restos embrionarios enclavados en cualquier punto orgánico. Es más curioso todavía preguntarse qué es lo que influye en la animación de esos restos en momentos tan opuestos de la vida. Nadie hasta ahora ha dado una respuesta satisfactoria y así debe ser por poco que se piense en ello, y si hemos recordado a nuestro turno estos hechos es por hábito bien entendido más que por otra cosa.

Nuestro enfermo, argentino agricultor, de 30 años de edad, carece de antecedentes patológicos hereditarios y personales. Su salud ha sido inalterable, sus ocupaciones de las más sanas. Ha enfermado una sola vez que ha sido aquélla que lo condujo a la muerte. Él comienzo de su enfermedad data de un año. Más que él, fué su familia la que se apercibió de ella. No se inició en una forma intensa ni se hizo visi-

ble por manifestaciones exteriores. Sus síntomas se refirieron a modificaciones del carácter. Estos correspondían a una pérdida de atención, memoria, discernimiento, es decir, de la inteligencia, a una disminución de la voluntad, y a la aparición de una tristeza, apatía, indiferencia y desgano crecientes. Este cortejo psíquico se acompañó de cefalia intermitente, de variable intensidad. Sus allegados creyeron que el enfermo simulaba una afección, con el propósito de eludir, quién sabe porqué, su trabajo. Mas como las perturbaciones cerebrales iban en aumento la cefalia aumentaba y acercaba sus accesos, y como se insinuaban otras anormalidades, v. gr., vómitos, convulsiones frustras de los miembros, anorexia, disminución de la visión en el ojo derecho, la familia se resolvió hacerlo examinar siendo rápidamente decidida a ello a causa de una serie de ataques que terminaron por una hemiplegia derecha.

Alojado en nuestra sala de hospital, se le hizo el examen de su estado y él no dió datos de mayor importancia, como puede verse más abajo, a no ser los que se refieren a la esfera nerviosa y a la visión.

Es un sujeto en buenas condiciones de nutrición, con buen desarrollo óseo y muscular y regular cantidad de panículo adiposo.

Cabeza: El sistema piloso y el cuero cabelludo son normales. El cráneo es mesocéfalo.

Ojos: No hay edema de los párpados; conjuntivas normales.

Nariz y oidos: Normales.

Boca: Lengua muy saburral.

Cuello: No se ven latidos arteriales ni se palpan ganglios.

Tórax: Cilíndrico; tipo respiratorio costoabdominal, 14 respiraciones por minuto.

Pulmones (por detrás): Excursión respiratoria normal. Existen vibraciones vocales normales desde el vértice hasta la base. Sonoridad normal en toda la superficie pulmonar. Murmullo vesicular normal. Por delante: idénticos fenómenos.

Corazón: La punta se ve y se palpa en el quinto espacio intercostal, siguiendo la línea mamilar; nada de particular a la palpación de la región precordial; la percusión denota que el area cardíaca es normal; auscultando se oyen los tonos normales en los cuatro focos.

Pulso: Frecuencia, 60 pulsaciones; buena tensión y expansión, regular, igual.

Abdomen: Inspección; nada de particular.

Palpación (hígado): El borde superior se percute en el quinto espacio intercostal en la línea mamilar, ocupando el resto del borde su sitio normal; el borde inferior se palpa a dos traveses de dedo por debajo del reborde costal. Esta hipertrofía del órgano es debida a la presencia de quistes hidáticos en la glándula.

Baso: La percusión descubre un ligero aumento de la matitez; se palpa en el hipocondrio izquierdo durante las profundas inspiraciones.

Riñones: No se palpan.

Nada de particular en el resto de las vísceras.

Órganos genitales: Testículos y epidídimos normales.

Miembros: No hay edemas.

Sistema nervioso (motilidad): La motilidad voluntaria de la pierna y braso derecho está completamente abolida. El braso cae doblado sobre el tronco y la pierna extendida sobre la cama. Los movimientos activos están imposibilitados, no puede levantar el braso, no puede caminar, no puede aprovechar el primero para los actos de la vida ordinaria y se vale para efectuarlos del braso y pierna izquierdos. La marcha es dificultosa; el enfermo no puede permanecer de pie y cuando camina arrastra la pierna derecha. De pie tiene tendencia a caer hacia atrás y a la derecha.

La lengua, dentro de la boca, está derecha, pero si se la hace proyectar fuera de ella, se desvía visiblemente hacia el lado derecho, vale decir, hacia el lado paralizado.

El velo del paladar se encuentra caído uniformemente sobre la lengua; por eso debe alimentarse lentamente y aún así suelen pasar con relativa frecuencia los alimentes a las fosas nasales, a consecuencia de lo cual hay serios trastornos de la deglución. Las

fauces no pueden examinarse prolijamente porque hay contractura de los maséteros, la cual pónese en evidencia si se pretende abrir la boca. La voz del enfermo es francamente gangosa.

Reflejos: Los reflejos cutáneos están exagerados. Hay fenómeno de Babinsky; si se excita la planta del pie del lado derecho, se observa que los dedos se flexionan hacia la planta, excepto del dedo gordo que se extiende.

Los reflejos tendinosos están exagerados; la percusión del tendón de Aquiles o del tendón rotuliano, produce una brusca extensión del pie y de la pierna, respectivamente. Hay además clonus y trepidación epileptoidea.

En el miembro superior derecho se observa el mismo fenómeno; la percusión de los tendones en cualquier punto que éstos estén a flor de piel, produce la exageración de los movimientos fisiológicos correspondientes.

Sensibilidad: Al tacto, dolor y calor conservada.

Atrofias musculares: Las eminencias tenar e hipotenar de la mano derecha se presentan deprimidas, debido a la atrofia de los músculos que las constituyen. Estas atrofias se observan también en el antebrazo al nivel de las eminencias epitroclear y epicondilea, como en el brazo. El miembro inferior derecho está igualmente atrofiado.

Accesos epileptiformes: En ciertos momentos, al practicarse el examen clínico, el cuerpo es sacudido por convulsiones de ritmo y mediana intensidad, precedidas de un grito semejante a un chillido.

Contracturas: Existe contractura de la mitad derecha del cuerpo, hay además rigidez de la nuca, columna vertebral y de los maséteros (trismus).

Examen de los aparatos sensoriales (sentido de la vista): No hay trastornos motores de los párpados. Hay anisocoria: la pupila derecha es más grande que la izquierda; la primera no reacciona a la luz. El examen del fondo del ojo descubre una atrofia de la pupila completa en el ojo derecho, menos pronunciada en el opuesto. A consecuencia de esto, la visión no existe en el primero. El ojo izquierdo presenta disminución concéntrica del campo visual y la visión está reducida al décimo. El sentido del olfato, gusto y oído es normal.

Examen psíquico: Su estado mental se presenta profundamente alterado. Ha perdido la atención y la memoria; desatiende la conversación y ha olvidado todo cuanto se refiere a su existencia. Vive en una perpetua somnolencia interrumpida a ratos por ligera animación. Estas deficiencias mentales se han ido acentuando progresivamente y hubiera sido fácil seguirlas, si el enfermo se hubiera recluído en el hospital desde los comienzos de su afección; no representan más que los últimos grados del estado psíquico que hemos descrito en los prodromos de su enfermedad.

Todos los signos clínicos que acabamos de enumerar parecen caracterizar un tumor de la fosa cerebral media. Que se trata de un tumor es lógico pensarlo, por la cefalia persistente, gravativa, intensa, los vómitos, por la ambliopía y la ceguera, por los trastornos epileptiformes y hemipléjicos y por la hipertensión del líquido céfalo-raquideo. Que esté localizado en la fosa cerebral media, es lo que vamos a demostrar, valiéndonos de algunos de esos síntomas y de los que caracterizan a los que tienen asiento en las otras dos fosas. Los tumores de la fosa cerebral anterior se distinguen por la anosmia, la ataxia de Bing y las perturbaciones psíquicas y la ausencia de atrofia de los nervios ópticos, mientras que los de la fosa cerebral posterior originan rigidez de la nuca, fenómenos de la ataxia cerebelosa, falta de reflejo corneal, parálisis del facial y del auditivo, verdadera triada patognomónica y además falta de atrofia de los nervios ópticos. Por este rápido análisis, queda suficientemente demostrada la localización mediana del tumor.

Los trastornos visuales tienen su punto de origen en la atrofia descendente de los nervios ópticos consecutiva a compresión producida por el tumor, una de cuyas porciones apoyaba sobre el quiasma y los nervios ópticos. La ceguera, como la ambliopía no han sido repentinas, sino que se han establecido paulatinamente y, es posible, que los ojos examinados en el comienzo de la enfermedad hubieren presentado un campo



FIGURA 1.—Tumor de la base, de forma prismática y del tamaño de una nuez; se insinúa hacia el interior de la masa encefálica, metiéndose como una cuña entre los dos hemisferios.

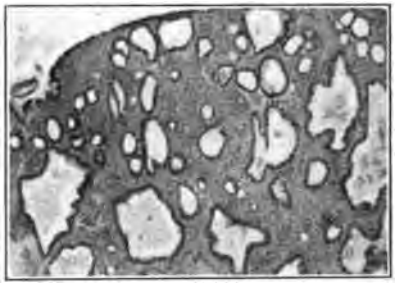


FIGURA 2.—Zona cortical del tumor en la que se observan los anchos cordones, circunscribiendo cavidades pequeñas e irregulares.

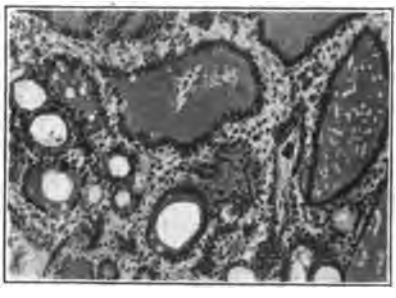


FIGURA 3.—El mismo campo que el anterior observado con gran aumento. Las cavidades están revestidas por una fina membrana colágena y, por fuera de ésta, la capa basal.

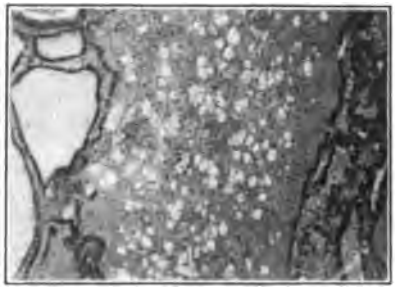


FIGURA 4.—Tejido especial constituído por sustancia fundamental pialina que encierra cavidades esféricas, dentro de las cuales existen elementos celulares. (Restos cordales.)

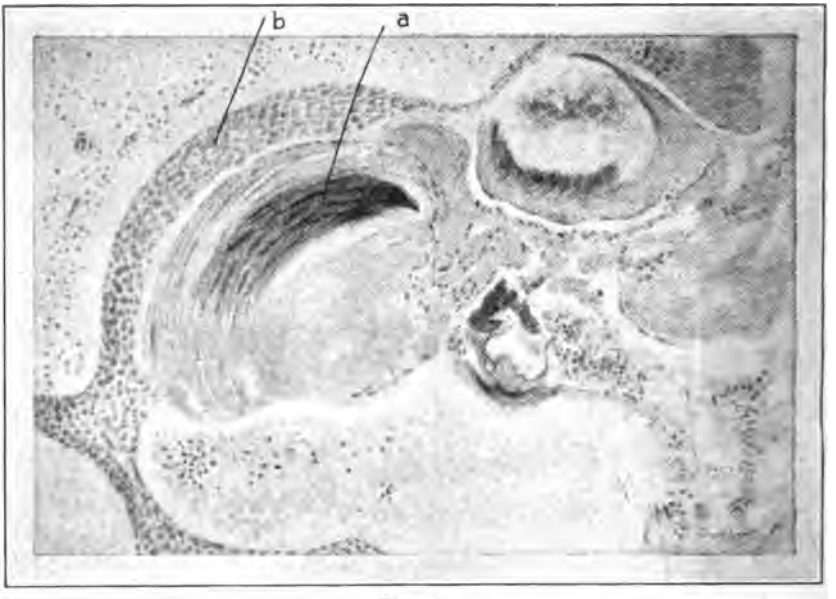


Figura 1.

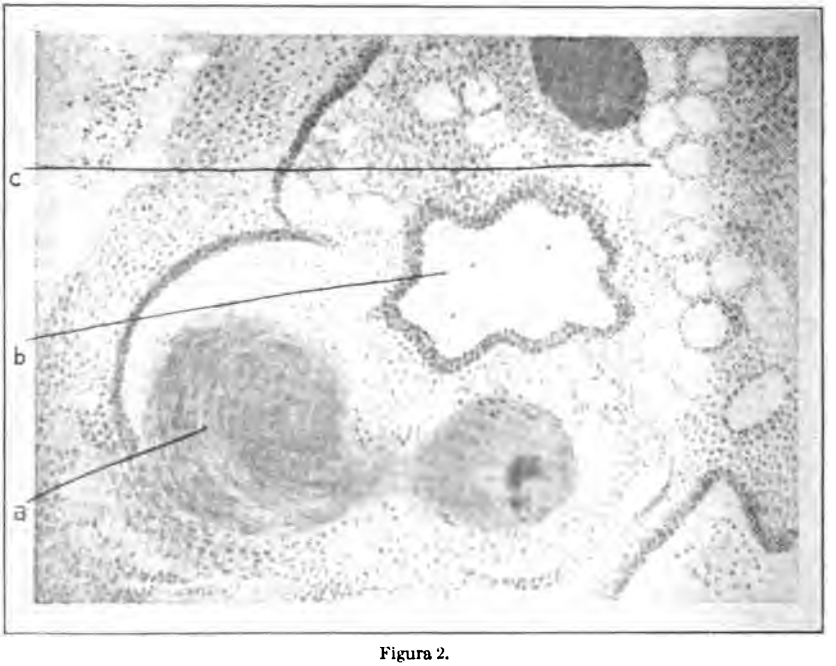


Figura 2.

LÁMINA A.

FIGURA 1.—(*a*) Formaciones córneas con incrustaciones córneas dándole el aspecto de laminillas óseas. (*b*) Cordón de células.

FIGURA 2.—(*a*) La misma apariencia anterior. (*b*) Formación hialina con escasas células rodeada por las células de los cordones y por un tejido arcolar (*c*) que recuerda el tejido grasoso.

visual con algunas de las modificaciones hemianópsicas conocidas. El campo visual del ojo izquierdo es el de una estrechez concéntrica del mismo sumamente avanzado, típica de la atrofia del nervio óptico; sólo quedaba respetada la visión macular y eso en forma bastante reducida puesto que el visum era igual al décimo del normal. La midriasis, como la falta de reacción de la pupila a la luz del ojo derecho, se explica por la amaurosis misma.

Los accesos epileptiformes tienen su explicación en la compresión indirecta que han sufrido las zonas rolándicas, precisamente por el desarrollo del tumor que se insinuaba cada vez más entre los hemisferios y trataba de desplazar lateralmente su masa.

En cuanto a la parálisis vesical y rectal, puede admitirse, de acuerdo con ciertas teorías modernas, que sea debida a compresiones sufridas indirectamente por los nucleos grises centrales, donde estarían localizados los centros motrices de los esfínteres.

El trismus es debido posiblemente a una compresión directa ejercida por el tumor mismo sobre el nervio maxilar inferior.

Antes de hacer la descripción del tumor, señalaremos el aspecto de una serie de cortes hechos sobre el mismo, uno de los cuales, el más característico de todos, es el adjunto (fig. 1).

Primer corte: El tumor da un prolongamiento quístico, cuyas paredes membranosas y espesadas han seguido exactamente el camino de la cinta olfativa, ensanchando el surco que separa las circunvoluciones por donde aquélla camina, alcanza la substancia gris del centro olfativo orbitario, destruyendo en parte la substancia gris y desplazando ligeramente las formaciones locales hacia la izquierda. Los cuernos frontales están dilatados; las venas ventriculares congestionadas.

Segundo corte: En la cara frontal del segundo corte, la prolongación quística es más evidente, es más amplia y su pared membranosa más espesada. En la base el cuerpo del tumor posee un aspecto múltiple y que, por otra parte, se repetirá en el resto del mismo: hay zonas de aspecto cartilaginoso, gelatinoso, hay zonas sólidas, ahuecadas, quísticas, unas revestidas de substancia coloidea, otras encerrando una substancia blanquecina, cuyo aspecto recuerda al de la cal apagada. Se encuentran también pequeños focos hemorrágicos. En la cara temporal del corte se ve una cavidad quística de paredes muy espesadas, limitando con los ventrículos laterales.

Tercer corte: La cavidad quística está más desarrollada que en ninguna otra parte; tiene una capacidad de una avellana. No ha invadido la substancia cerebral. La membrana que es más espesa a medida que nos acercamos a la base del tumor, está aplicada sobre aquélla y en su crecimiento se ha adaptado exactamente a la superficie cerebral, de modo que presenta una serie de dobleces o crestas dirigidas en el sentido anteroposterior. Esa cavidad quística se ha desarrollado hacia la derecha y por consiguiente ha comprimido la masa cerebral.

Sobre la cara occipital del mismo corte, se ve una pequeña cantidad de contenido coloideo, revestida de una membrana que tiene el aspecto de la anterior, independiente de la misma, y que ha rechazado la mitad izquierda de la comisura blanca anterior, y que hace hernia en la cavidad del ventrículo.

Cuarto corte: En la porción más posterior hay una membrana quística que comprime el pie del pedúnculo.

En resumen, el tumor es una formación prismática, cuyas dimensiones son las siguientes: largo 4 centímetros, ancho 2 centímetros, altura, en su parte media, 3 centímetros. Lateralmente está limitado por los lados del ángulo que forman los pedúnculos y por los bordes internos de los lóbulos témporo esfenoidales; por su cara inferior, descansa sobre la silla turca; por su cara superior llega hasta la base del tercer ventrículo. En su crecimiento ha alcanzado a destruir las formaciones blancas y grises situadas en el espacio cuadrangular, delimitado por las cintillas ópticas y por los pedúnculos y ocupado por los tubérculos cuadrigéminos y tuber cinereum. Sus caras son mamelonadas, tienen el color de la substancia cerebral, están recorridas por

escasos capilares. En la masa del tumor hay, como se ha señalado más arriba con mayores detalles, algunas formaciones quísticas de variado aspecto, con incrustaciones blanquiscas, ásperas, como si fueran de polvo calcaéro.

Es necesario, para comprender algunos síntomas clínicos que, estando el límite posterior del tumor por delante del origen aparente del tercer par craneano, ningún centro nuclear del mesencéfalo ha sido tomado y, como el tumor se ha desarrollado hacia el interior de la masa encefálica, metiéndose como una cuña entre los hemisferios las fibras radiculares de los nervios en especial de aquéllos que se dirigen al ojo, han sido respetados. La amaurosis de uno de los ojos se explica por la compresión y destrucción sufrida por el quiasma. La parálisis derecha es debida a la compresión del pedúnculo cerebral del lado izquierdo.

El estudio histológico de la neoplasia nos ha dado el siguiente resultado (fig. 1).

El tumor está constituído por cordones de células de espesor variable, finos en unos lugares, gruesos en otros y que, al encontrarse circunscriben cavidades y fisuras de contornos y volumen variables, siendo las pequeñas corticales y las mayores centrales.

Los cordones están formados por células de forma variable, presionadas mutuamente, sin cemento intercelular y unidas entre sí por filamentos que recuerdan las que yacen en el cuerpo mucoso de Malpighi (Lámina A). Estos cordones están revestidos en su periferia por una hilera de células cúbicas, de núcleo central, tapizadas a su vez, por una membrana anhista uniforme y delgada (fig. 3). Las células poseen escaso protoplasma cuyo núcleo corresponde a la forma celular. Fácil es comprobar que la naturaleza de las células cordonales y de las cúbicas es epitelial. Los cordones son avasculares; hay uno que otro esbozo de vaso generalmente una fisura con o sin glóbulos rojos.

Las cavidades que delimitan las membranas basales contienen, unas, globos esféricos de substancia, aspecto y reacción de substancia coloidea; otras tienen substancia colidea uniforme o vacuolada, otras poseen además de esta substancia finos filamentos colágenos en contacto con la basal; otras están llenas de tejido hialino atravesado por vasos con paredes colágenas y presentando espacios vacíos que encierran grandes células mononucleadas, de núcleo pequeño. En algunos puntos estas formaciones son más densas; las células están dispuestas en cavidades hechas en plena substancia hialina que por el conjunto toma el aspecto de cartílago; sin embargo las células llenan completamente las cavidades que les dan alojamiento: su núcleo es pequeño, su protoplasma está formado por una fina red.

En otras zonas, inmediatamente por dentro de la membrana basal, hay un tejido conjuntivo de franco carácter colágeno, rico en células redondas y fusiformes. El resto del tejido está dispuesto en forma de areolas que recuerdan el grasoso.

En el espesor de los cordones epiteliales nótanse algunas formaciones globulares, en que hay elementos aplanados superpuestos formando capas concéntricas, como globos epidérmicos, por aplanamiento y transformación cornea de los elementos de los cordones. También en ellas se encuentran depósitos calcáreos.

Existe, por último, en menor proporción que las citadas formaciones, un tejido especial constituído por substancia fundamental hialina en partes, y en otras finamente granulosa, que encierra cavidades pequeñas, esféricas o irregulares por presión recíproca, dentro de las cuales encontramos células de protoplasma esponjoso y núcleo pequeño en relación al tamaño celular. Estas células no existen en todas las cavidades y la mayor parte no alcanzan a colmarlas, presentando entonces un protoplasma retraído o dentellado (fig. 4). Parecería, a primera vista, encontrarnos en presencia de formación cartilaginosa, pero el examen atento y las reacciones tintoriales nos demuestran que no es así.

Si comparamos esta formación con los datos obtenidos de la embriología, y recordamos la estructura de los tumores congénitos descritos por el Profesor Ribbert con el nombre de cordomas, aceptamos que ella está formada a expensas de restos cordales. La explicación embriogénica procede de la relación que tiene la extremidad anterior de la corda dorsalis con la membrana faringea en la base del encéfalo para formar la bolsa de Rathke.

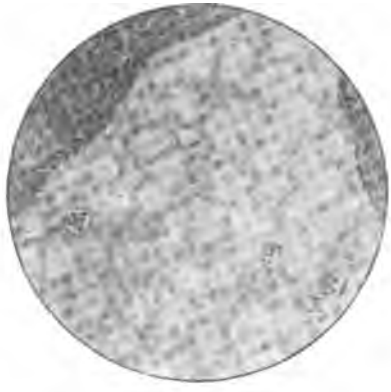


Figura 4.



Figura 3.



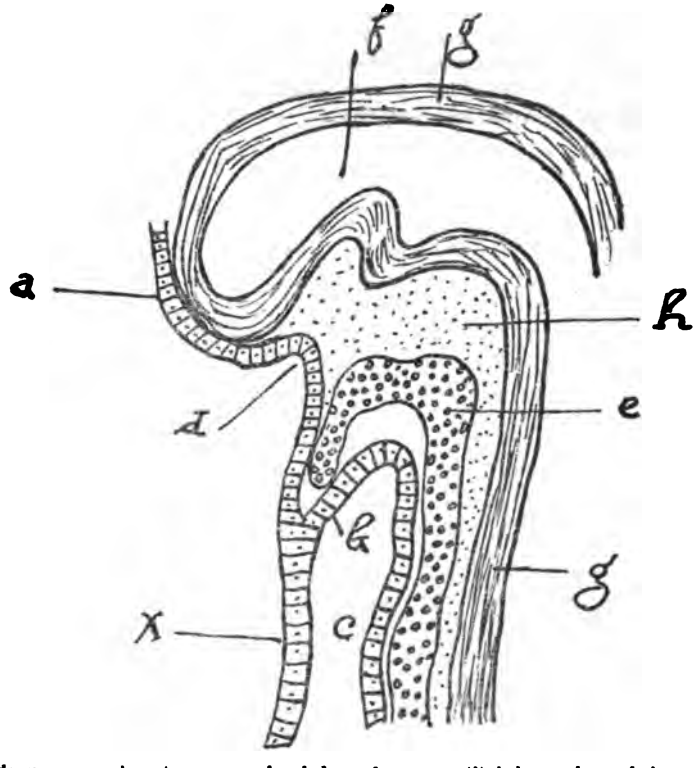
Figura 5.

LÁMINA B.

FIGURA 3.—Corte con gran aumento de cordones, mostrando los filamentos de unión entre los cordones.
FIGURA 4.—Tejido hialino conteniendo cavidades dentro de las cuales se encuentran mononucleadas de escaso protoplasma y que recuerdan la corda dorsalis.
FIGURA 5.—Formaciones calcáreas dispuestas en forma concéntrica semejando al colestratoma.

Respecto de las formaciones hialinas y coloideas que se interponen entre los cordones de la neoplasia, su interpretación es la siguiente: a primer golpe de vista, parecería que esas substancias fuesen una secreción de la capa de células cúbicas que ocupan la parte más externa de los cordones, recordando el aspecto de los cistomas en general; pero la franca limitación de los cordones que están revestidos por una membrana anhista cuya reacción colágena es evidente y que en algunos puntos está constituída por un acúmulo de fibrillas de igual naturaleza, aleja esta concepción.

De modo pues, que por fuera de la membrana basal constituída por las células cúbicas, existe como si dijéramos un dermis, cuya estructura es varia y que ha sufrido



a—ectodermo que en el punto x se une al endodermo b para constituir la membrana faringea.
c—faringe o intestino anterior.
d—bolsa o divertículo de Rathke.
e—corda dorsalis que se insinúa en su extremidad anterior entre las dos láminas a y b de la membrana faringea.
f—cavidad cerebral.
g—tejido nervioso que la forma.
h—mesodermo.

una transformación hialina o coloidea, viéndose su carácter fibrilar en pocos lugares.

Para interpretar la histogénesis de este tumor, hay que remontarse al período embrionario. Es sabido que la membrana faringea, antes de su perforación forma en la base cefálica un divertículo llamado la bolsa de Rathke. Esta ha de constituir ulteriormente la hipófisis y, aquélla, a expensas de la cual se hace el divertículo de que hablamos, consta, de ectodermo y endodermo. Ahora bien, la corda dorsalis formación ectodérmica que está por delante del neuro—eje termina en su porción anterior juxta—poniéndose a la capa ectodérmica de la membrana faringea e insinuándose entre ésta y la capa endodérmica. Así, podríamos explicar que elementos de la corda dorsalis

puedan ser arrastrados con el divertículo, e incluídos en el vástago e infundíbulo de la hipófisis, den lugar a este tumor complejo que estudiamos.

El caso que estudiamos es análogo al relatado por el Profesor Yutaka Kohn del Instituto de Anatomía Patológica de Munich y clasificado por éste con el nombre de teratoma, en el cual había además formaciones cartilaginosas y óseas que no existen en el nuestro.

Se trata, entonces, de un tumor de naturaleza epitelial, formado a expensas de la membrana faringea, cuando ésta se invagina para forma la hipófisis. Algunos elementos de esta membrana unidos con restos de la corda, cuya relación con la membrana faringea puede apercibirse en el esquema adjunto, han quedado aislados y alojados dentro de la cavidad craneana, dando lugar al desarrollo de la neoplasia.

El tumor está formado, en consecuencia, por elementos ectodérmicos, mesodérmicos y endodérmicos; los primeros constituyendo el ectodermo general del embrión que entra a forma parte de la membrana faringea; los segundos por los elementos conjuntivos que se ven en él; y, los terceros, constituídos por las formaciones cordales que, como es sabido, derivan del ectodermo.

Adjournment.

GENERAL SESSION OF SECTION VIII.

NEW EBBITT HOTEL,
Friday morning, January 7, 1916.

Chairman, R. H. CARTER.

The session was called to order at 9.15 o'clock by the chairman.

The CHAIRMAN. The first paper this morning is by Dr. Calkins, of Columbia University, on "General biology of the protozoan life cycle."

GENERAL BIOLOGY OF THE PROTOZOAN LIFE CYCLE.

By GARY N. CALKINS,
Professor of Protozoology in Columbia University.

For five decades after the time of Ehrenberg the peculiar conception of a protozoan as a miniature replica of a metazoan, held by this gifted observer, influenced the study of protozoa. This influence gradually wore off and, so far as morphology is concerned, ended with the careful observations of Stein, Claparède and Lachmann, Engelmann, Bütschli, and Hertwig, who showed that various structures of the protozoan body are not beating hearts, brains, ovaries, and stomachs, but are simple differentiations of the single-celled organisms.

A more lasting influence of Ehrenberg's teaching, seen even to-day, is the habit of regarding a single protozoon as the complete expression of a species equivalent to an individual worm, mollusc or mammal. The individual metazoon dies, while the protozoon does not die, but grows to full size and divides into two or more—facts which led Weismann to his conclusions regarding mortality in metazoa and immortality in protozoa.

We owe to Maupas the credit for dissipating this last reminiscence of Ehrenberg's teaching, and for showing that the single cell is not the final representative of a protozoon species. We are accustomed to the idea that many individuals of a polymorphic coelenterate are present in potential in the fertilized egg of the coelenterate, but we are less accustomed to the idea that polymorphic individuals are present in potential, in the fertilized cell of a protozoon. Research in recent years has shown that successive generations of protozoa may be more or less progressively differentiated, so that a cell picked out at one phase of the life cycle is quite a different type of individual from one picked out at another phase. Which, for example, would be the "type" individual of the dimorphic Foraminifera? Which would be the type in the reproducing flagellated and ameboid stages of *Nägleria punctata*? of different phases in the life history of *Centropyxis*, *Arcella*, or *Difflugia*? or of intestinal and blood-dwelling stages of *Plasmodium*? The morphological differences here indicate that the protozoan life history involves differentiation analogous to that of a polymorphic metazoon, and justify the comparison of the whole life cycle with the development and differentiation of a metazoon, especially that of a metagenetic type such as coelenterate or trematode.

The importance of the whole life cycle, first demonstrated by Maupas, was fully recognized by Schaudinn and applied by him to the study of parasitic forms. The monographs resulting from this study, especially those on *Coccidium schubergi*, *Plasmodium vivax*, and on rhizopods, are classics in the literature of protozoa, and models which later students have followed.

Through Schaudinn's work, and by later researches, the sequence of events in different parasitic types has been made out with painstaking care until to-day we know the general history of the majority of injurious human protozoan parasites, the modes of transmission from host to host, the types of intermediate hosts and what happens in them. In short, we know enough to furnish an adequate basis for public and private prophylaxis which, in the hands of sanitary commissioners and public-health officers, has put an end to epidemics of yellow fever, malaria, and dysentery; has rehabilitated vast tracts of land in Italy; saved millions of dollars in South Africa and in our Southern States; and has made the Panama Canal possible.

Such are the first and practically the most important results of our knowledge concerning protozoan life cycles; quite enough, indeed, to justify the science of protozoology. Important as these results are, we are not at all satisfied; we know too little about the conditions of development; too little about the nature of the vital processes of the organisms themselves and their variations in structure and function under differing conditions—ignorance which must be cleared away before much further practical advance can be made. Further advance will be less spectacular and must be based upon the biological study of the organisms as units of protoplasmic substance, and this will rest upon working hypotheses supported by experiment. It is along such theoretical lines that I wish to direct your attention for a few minutes, to develop a conception of the life cycle as a whole, and to offer a theoretical interpretation of the different phases of vitality and of structural variations.

Let us consider for a moment a single *Ameba*, or a malaria germ, not as a cause of disease, but as a unit mass of protoplasm which, like a free-living *Paramecium* or *Didinium*, performs all of the fundamental vital activities common to living things—namely, nutrition, excretion, irritability, and reproduction. The chemical composition of these unit masses, so far as I know, has never been made out, but there is no reason to doubt that it agrees with that of other living substances, since the accompanying properties of protoplasm—metabolism, growth, and reproduction—are obviously performed, and probably in the same way. In such unit masses of protoplasm we assume that processes of hydrolysis, synthesis, oxidation, and reduction are constantly going on as in other protoplasms, and not in any haphazard way, but always orderly and under regulative control of the organism as a whole. The appearance of *Ameba* shows that the protoplasm is made up of alveoli and interalveolar substances of different density, representing colloidal and crystalloidal substances in a general mixture which Ostwald describes as an emulsoid. Between these different substances constant chemical activities are in progress, and the orderliness which distinguishes these processes in the protoplasm of the living organism from similar processes which go on in the same protoplasm when crushed, are possibly due, as Mathews states, to the physical barriers of cellular and nuclear membranes, alveoli, and the colloidal centers of activity. The speed with which such processes take place in living protoplasm, which, in itself, distinguishes living processes from chemical processes in lifeless substances, is due to specific enzymes or catalyzers which are manufactured as a result of chemical activities in living protoplasm. These bring about and control each successive step in the long chain of chemical actions involved in destructive metabolism, the action in each event being conditioned by the nature of the protoplasmic substratum. In this chain of destructive processes different substances may be formed which undergo no further oxidation or other chemical change, but are stored up in the protoplasm until disposed of by excretion, these products, leading to changes in the protoplasmic substratum—i. e., to protoplasmic

chemical differentiation—may or may not be accompanied by visible structural differentiations. Such products of destructive metabolism, in the form usually of nucleo-

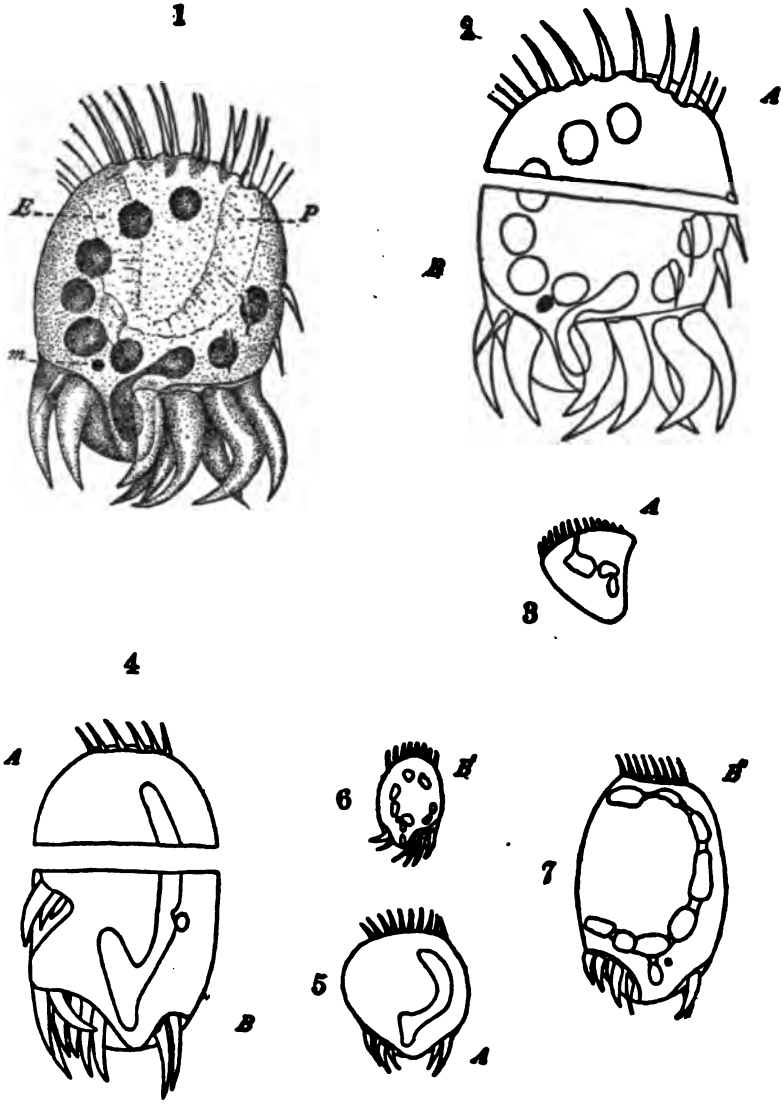


FIG. 1. Normal adult individual of *Uronychia transfuga* with macro-nucleus in the form of large chromatin spherules; micronucleus (*m*); endoral membrane (*E*); pre-oral membrane (*P*); and large posterior cirri.

FIGS. 2 AND 3. Individual 12 hours old cut as shown in 2. Part *A* had no micronucleus and after 72 hours appeared as shown in 3 *A*. Part *B* regenerated perfectly in 24 hours.

FIGS. 4, 5, 6 AND 7. Individual cut at age of 24 hours as shown in 4. *A* regenerated perfectly, except for absence of micronucleus, in 24 hours (5 *A*); *B* divided through the original division plane (indicated in 4), within a few hours forming a minute but perfect individual (6*B'*), and a normal full-size individual (7*B''*).

proteins or their derivatives, may act as poisons to other organisms, as melanin does to the host in malaria, or as the proteolytic ferments of *Entameba histolytica* do in

dysentery; or they may play some important part in the vital activities of the organism itself, as in phosphorescence of *Noctiluca* and the dinoflagellates, or, more generally, in regeneration and reproduction.

Let me illustrate this latter point by some experiments made on *Uronychia transfuga*, a ciliated protozoon. This organism has rather a complicated structure with nine giant cirri at the posterior end. Under laboratory conditions it divides once a day approximately, or, more exactly, once in 26 hours. The first indication of division, is the precocious formation of the giant cirri in a central region of the body which we have called the "division zone." The experiments were undertaken for the purpose of studying the relative power of regeneration of the single cell at different ages between divisions, it having first been determined that the cell regenerates readily after being cut. Cells were cut with a scalpel at different periods subsequent to division; some during the end stages of division; some 15 minutes after division; some one hour after; others 2, 4, 8, 12, 16, and 20 hours after, and some were cut just prior to the next division period—i. e., 24 to 25 hours after division. In all cases of record the cells were so cut that one portion contained the micronucleus and part of the macronucleus, the other portion containing only a part of the macronucleus. The former, or, as I shall call it, the nucleated portion, invariably regenerated after some hours, forming a perfect cell; the latter, without a micronucleus, which I shall call the enucleated portion, behaved differently as regards regeneration, according to the age of the cell when cut. In all cases this portion lived from three to five days after the operation. If the recently divided cell were cut at any period up to 16 hours after division the result was the same; no regeneration occurred, the fragment merely rounded out, swimming about by its adoral membranelles. If the cells were cut when from 18 to 24 hours old, regeneration occurred not only in the nucleated portion, but in the enucleated fragment as well, the percentage of regeneration increasing with the increased age of the cells when cut, until at the age of 24 to 25 hours the enucleated fragments regenerated perfectly in 100 per cent of cases.

These results indicate a gradual chemical differentiation of the protoplasm as a result probably of destructive and constructive metabolic processes. The giant cirri which are regenerated are the visible expression of inherited structures characteristic of the species. Since the enucleated fragment from a cell cut when young does not regenerate while the nucleated fragment does, we must conclude that one essential factor at least, necessary for the production of these inherited structures, lies in the micronucleus.

The giant cirri, furthermore, are visible differentiations which are precociously formed at division. This must mean that the inherited factors find their expression at this period, and it follows from the successful formation of giant cirri in enucleate fragments from old cells that whatever may be the direct causative agent or agents in the process they must be generally distributed throughout the protoplasm at this time. We have no direct evidence as to what these agents may be. Possibly there is only one, and that of the nature of a specific enzyme, or perhaps some chemical body analogous to hormones formed as a result of mutual interaction of nucleus and cytoplasm when the latter has reached a certain stage of chemical differentiation through normal activities. Or it is possible that such chemical bodies are present at all times and are activated only when the protoplasmic substratum reaches some particular stage of development. Thus it is possible that, with continued metabolism, the acidity if the protoplasm gradually increases until a concentration is reached in which specific enzymes, not able to act before, are now activated.

However theoretical the interpretation of the phenomenon may be, the periodic and temporary power of regeneration is an observed fact, indicating a difference in the protoplasmic make-up at different age periods, a difference which may be satisfactorily expressed by the phrase cumulative chemical differentiation.

Another observed fact is that the regenerative power is exhausted with cell division, for young enucleated fragments do not regenerate. This indicates a reduction of the differentiated adult protoplasm to the condition of young cells; or, at least, the protoplasm is restored to a state where the causes underlying regeneration are inactive. This may be due to the exhaustion of specific substances which take part in the reaction of regeneration, or it may be due to the chemical and physical changes accompanying cell division.

We are led through these experiments to further speculations concerning the nature of cell division. Chemical differentiation of the protoplasm continues even after the stage is reached when regeneration is possible. This is shown by the fact that formation of the cirri in *Uronychia* precedes the process of division in normal cells, and by the additional fact that regeneration of cirri occurs while cell division does not occur in enucleate fragments cut from old cells. I would interpret cell division as due to cytolytic action set up by enzymes or other chemical bodies produced as a result of interaction of nucleus and cell body differentiated chemically by age. Cytolysis may then occur more or less extensively throughout the entire protoplasmic mass, but it is most active in the division zone of the organism which is more highly differentiated than other regions (see Calkins, 1911, and Peebles, 1912). The membrane of the cell turns in at this cytolyzed division, and the constriction results in cell division.

As a consequence of the activities accompanying cell division the protoplasmic substratum is reduced from the differentiated adult condition to the condition characteristic of young cells, and the process of growth and chemical differentiation, division, and dedifferentiation recur in more or less rhythmical succession.

Viewing the life cycle as a whole, there are two phases which must be taken into account. These are, first, the encystment phase, and, second, the sexual or conjugation phase, both widespread and almost universal in protozoan life histories. Let us first consider the encystment phase.

Encystment occurs ordinarily when the conditions in the surrounding medium are adverse, such as desiccation, lack of food, etc., such encysted forms emerging from the cyst when suitable conditions are restored. In some cases, also, encystment occurs during the digestion of food. In addition to these casual encystments there is another form of encystment which involves more deeply lying activities of the protoplasm. In *Didinium nasutum* I have found that encystment occurs at periodic intervals which can not in any way be connected with adverse conditions of the environment or with feeding, but must be interpreted as a normal phenomenon due to internal conditions of the organisms. Encystment at such times persists for from five to eight days, and during this period no amount of coaxing will bring the organisms out. During such encystment the macronucleus fragments into hundreds of small chromatin particles, which are ultimately absorbed in the cytoplasm. The micronuclei divide, and products of their division give rise to a new macronucleus and new micronuclei. When the process is completed and the organisms emerge from their cysts, they possess from five to seven times the vitality, as measured by the division rate, of the same race prior to encystment. Fermor was the first in 1913 to describe similar happenings during the encystment of *Stylonychia*. In this case dissolution of the old macronucleus and absorption of the fragments, fusion of the two micronuclei, and formation of new macronuclei and micronuclei from the fusion nucleus were described.

It is well known that *Paramecium* does not encyst. Nevertheless Woodruff and Erdmann (1914) have shown that phenomena similar to those occurring during encystment in *Stylonychia* and *Didinium*, and which they refer to under the general term "endomixis," recur at periodic intervals (about once a month) in the case of *Paramecium aurelia*. Here also the old macronucleus fragments and the fragments are

absorbed in the cytoplasm, while a new macronucleus and micronuclei are formed from the division products of the micronuclei.

The interpretation of this set of phenomena in the life history of protozoa is a perplexing problem. There is not a doubt that vitality, as measured by the division rate, is restored. Likewise there is little reasonable doubt that a complete chemical and physical reorganization of the protoplasm takes place. The renewal of vitality was shown both in Woodruff's culture and in my *Didinium* culture, and one general problem is stated in the query: How long can such periods of reorganization continue? Woodruff believes that they may keep on indefinitely, but in my experiments with *Didinium* the race apparently lost its power to encyst and ultimately died out after six months' culture without encystment. So too, in my culture of *Paramecium caudatum* (1902), where similar reorganization occurred at least twice, the race ultimately lost the power to reorganize and died out. I may have had unfavorable forms to start with and so lost both races at early dates. It is interesting in this connection, however, to note that Whitney, working with the rotifer *Hydatina*, a metazoon, carried a race through nearly 200 generations by parthenogenesis when the individuals lost their power to reproduce in this way, and many of his lines died, while others produced sexual individuals.

The general bioligical effect of this process of reorganization is a new chemical combination with a new potential of metabolic activity, and a new lease of life. Not only are the nuclei restored to activity, but the cytoplasm is likewise completely reorganized by the distribution through it of relatively large quantities of nucleoproteins, giving rise to successive derivatives (through hydrolysis, oxidation, reduction, etc.), all increasing the metabolic processes and releasing more chemical energy expressed by activity of movement and feeding, and leading to more rapid assimilation and growth, all indicated by an increased division rate. In short, the protoplasm is rejuvenated.

The second phase in the life history to be considered—viz, the sexual phase—involves still more deeply reaching protoplasmic activities. The protoplasm of the individual cells at this period has a different physical, and presumably chemical, make up than during ordinary vegetative periods. In free-living forms, such as the ciliates, the outer protoplasm becomes sticky or glutinous, so that two cells, on touching, fuse together. In this condition, which I have called the "miscible state," conjugation is possible, and the physical condition may be so extreme that groups of cells get stuck together. I have witnessed the fusion of nine *Paramecium caudatum* cells in a single amorphous mass.

In other forms—notably the parasitic protozoa—protoplasmic changes at this stage follow two lines of differentiation. Some cells store up metabolic products in the form of reserves of nutriment and develop into female gametocytes or macrogametes. Others develop into more active male gametocytes and microgametes. In both of these differentiated types if union or fertilization is prevented, the cells die a natural death.

The effects of conjugation or fertilization are almost the same as those following asexual reorganization through encystment. In ciliates cytolysis of the old macronucleus takes place and its substances are absorbed—that is, undergo chemical changes in the cytoplasm. The majority of the maturation nuclei, both in free-living and in parasitic forms, meet the same fate, while a new nuclear apparatus results from the products of the fertilization nucleus or synkaryon. The cytoplasm is renewed in a chemical sense and metabolic activities recommence with renewed vigor; a new race is started. The sole difference from encystment is that reorganization occurs after or during amphimixis, and a new hereditary complex is formed in the nucleus, while even this, in endogamous conjugation at least, can not be very different from the condition after asexual reorganization. It is obvious that, if conjugation is the

equivalent of fertilization in metazoa, asexual reorganization or endomixis is the equivalent of parthenogenesis.

What is the significance of these two important phases in the life cycle and how can they be interpreted in terms of metabolic activities? As we have seen, there is reason to believe that the cell protoplasm becomes progressively differentiated in a chemical sense between division periods, until just prior to division processes take place which do not occur at earlier periods. With division this differentiated condition is reduced, possibly through cytolysis, until a more labile protoplasm results. Now it is not at all improbable that such reducing processes are more or less incomplete, so that the protoplasmic substratum in the second generation is different from that of the first. We have evidence of this in the foraminifera where differences in the protoplasmic structure and in shell structure characterize the second generation. Further evidence is seen in the rhizopods, where increasing quantities of chromidia, and in some cases differences in shell structure, are morphological indications of differentiation.

Furthermore, it is not improbable that such differences are cumulative from generation to generation, just as chemical differentiation is cumulative with inter-divisional age, until a protoplasmic substratum is evolved in which processes not possible before can now take place. We have shown that *Paramecium* at the conjugation phase has a different physical make-up than at other times, the cortical plasm becomes mucilaginous and fusion results on contact, while physiological differences are manifested by the invariably decreasing division rate during and after this period when conjugation is possible. Here the protoplasmic substratum is differentiated, and processes occur which are not possible at other times. So, too, in *Didinium*, *Stylonychia*, etc., with successive generations, a protoplasmic substratum is gradually evolved (possibly hastened by adverse conditions) in which the peripheral zone of protoplasm undergoes cytolysis and forms an impervious membrane—the cyst membrane—analogous to the fertilization membranes of metazoan eggs. Further cytolytic changes, involving hydrolysis, reduction, and other chemical activities, are set up in the cell body, especially in the cell nuclei which divide or fragment. As a result of these activities, which are more profound than those accompanying cell division, the protoplasm is again restored to a labile condition, vitality is renewed and a de-differentiated protoplasm begins a new cycle of metabolic and reproductive phases.

The phenomena of conjugation may be interpreted in a similar way as due to processes possible only in a substratum produced by cumulative protoplasmic differentiation. A visible expression of such differentiation is seen again in chromidia formation of *Sarcodina* and in the dimorphic gametocytes of foraminifera and Sporozoa. The reorganization phenomena are quite as complicated and as far reaching as after encystment, and the end result is the same, a de-differentiated protoplasm and a new individual with a high potential of vitality. If fertilization is prevented the differentiated macro and microgametes die as do metazoan eggs and spermatozoa, and a similar result follows the continued culture of free-living ciliates, in which conjugation, or its equivalent, asexual endomixis, is prevented.

In all life histories we find more or less regular cycles of vegetative and sexual phases, complicated by more or less active asexual and sexual reproduction. In parasitic forms it is possible, I may say probable, that reorganization and renewal of vitality take place during encysted stages as Schaudinn, Wenyon, and others have held for the genus *Entameba;* or, as in *Paramecium*, they may take place without encystment in types like *Plasmodium* as described by Schaudinn. The processes of autogamy, so called, described for different types of *Entameba*, may be interpreted as asexual endomixis, and the conflicting views as to the significance of nuclear structures in *Entameba coli*, *E. histolytica*, *E. tetragena*, and *E. minuta* may all be reconciled when this possibility of asexual reorganization is applied to the various parasitic rhizopods.

With *Plasmodium* the principle of asexual reorganization and renewal of vitality, or parthenogenesis, has long been called upon to explain malaria relapse. The process, as described by Schaudinn, is too familar to need repetition here. Despite the objections which have been raised in recent years against this interpretation, it must be admitted that no a priori difficulty stands in its way. It is evident from experiments that the protoplasm of an old race is more stabile than that of a young race, possibly due to accumulation of products of metabolism in the former, either for a useful purpose, as in the storage of yolk material in a female cell, or for some harmful purpose, as in *Paramecium caudatum* during depression. In either case if a labile protoplasm can be restored resulting in chemical activities which ultimately bring about dissolution of these formed products, then renewed vitality is the outcome. Asexual reorganization effects this result, but the same result was produced artificially by the use of salts in my experiments with *Paramecium caudatum* during conditions of depression, and in cases where the cell body was visibly loaded with products which it could not automatically dispose of. The splendid results which Bass has obtained in cultivating *Plasmodium* in vitro and in the presence of sugar indicate the possibility of malaria organisms while in a stabile condition being similarly changed into a labile condition by changes in the blood content of the host. Changes thus set up might well be the equivalent of asexual reorganization or parthenogenesis, or the equivalent of fertilization in restoring vitality.

In this sketch of the protozoan life cycle I have endeavored to give a comprehensive, though somewhat speculative, account of the different phases of vitality which may apply equally well to any type of protozoa. Cell division, reorganizing encystment or its equivalent, and conjugation, are all regarded as phenomena of the same general character, but differing in degree, the effect in each step being the restoration of the protoplasm to a condition more or less free from cumulative metabolic differentiations.

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Dr. GARY N. CALKINS took the chair.

The CHAIRMAN. The second paper on the program this morning is "Classification of parasitic amœbæ of man," by Capt. Craig. In the absence of Capt. Craig, an abstract of his paper will be read by Mr. Bowles.

THE CLASSIFICATION OF THE PARASITIC AMEBÆ OF MAN.

By CHARLES F. CRAIG,

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The classification of the amebæ has always been a most difficult problem, owing to our lack of knowledge of the complete life cycle of many of the so-called species;

the simple morphology of these organisms; the difficulties inherent in the study of such delicate cells with the staining methods at our command; and the conflicting opinions of protozoologists as to the data upon which generic and specific classification should be based. However, during recent years enough accurate data has been collected regarding amebæ to make it possible to divide them into several genera and species and classifications have been published by Chatton,[1] Alexieff,[2] Doflein,[3] Hartmann,[4] and Calkins.[5]

While none of the classifications so far published can be considered as final, for all classification must remain tentative until the entire life cycle of every organism contained in the individual classification is known, I believe that the one adopted by Calkins is the most logical, and it is the one that I shall employ in discussing the subject of the present paper. Further research will undoubtedly render it necessary to transfer species from one genus to another and probably new genera will be discovered, but Calkins's classification furnishes an excellent working basis for the differentiation of amebæ, and if followed will result in great good in clearing up the chaotic condition in which the study of these organisms has remained for so long.

Calkins divides the genus *Ameba* into seven genera, as follows: *Ameba*, *Vahlkampfia*, *Nagleria*, *Craigia*, *Trimastigameba*, *Entameba*, and *Parameba*. The generic name, *Entameba*, should, by law of priority, be spelled *Endameba*, for the reason given later in the discussion of this genus.

Of the seven genera mentioned above, only three are of interest to us in the consideration of the parasitic amebæ of man—i. e., *Vahlkampfia*, *Craigia*, and *Endameba*. Of these, *Craigia* and *Endameba* contain only true parasitic species, while *Vahlkampfia* contains species which may become parasitic under certain conditions and for a limited period of time.

GENUS VAHLKAMPFIA CHATTON 1912, EMEND CALKINS 1912.

In this genus are placed certain species of amebæ belonging to the "limax" group and which have no flagellate stage of development. Calkins thus defines the characteristics of this genus:[6]

> Minute free-living or commensal rhizopods moving as a finger-formed single pseudopodium or with irregular ectoplasmic outbursts to form a local or general hyaline ectoplasm. The nucleus is single or double, with finely divided chromatin forming a membrane like contour and with a definite karyosome. Reproduction by simple division, the karyosome dividing first like the nucleus-centrosome of Euglena, the peripheral chromatin forming the nuclear plate (Promitosis of Nagler). Cysts uninucleate. Food bacteria; habitat usually fresh water in ponds, etc., but many types are found in garden earth and some may be marine.

To the characteristics of the genus given above the following may be added: Most of the species, if not all, may be cultivated upon artificial media, and upon certain media the trophozoites and cysts may contain several nuclei, as proven by Calkins and Williams.[7] In addition to the habitats given by Calkins, it is now well demonstrated that certain species belonging to this genus may occasionally be parasitic in man and other animals for a limited period of time.

This genus is chiefly of interest to the medical protozoologist, because certain species belonging to it may often be cultivated from fecal material or liver abscess pus obtained from man, and hence be confused with the true parasitic amebæ or enda-

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[1] Bull. Soc. path. exot., 1912, v. 13.
[2] Bull. Soc. zool. de France, 1912, v. 55.
[3] Lehrbuch der Protozoenkunde. Edit. 2, 1911, 560.
[4] Handbuch der Path. Protozoen. V Prowazek, 1912, i, 51.
[5] Tr. 15th Internat. Cong. Hyg. and Demog., 1912, ii, 287.
[6] Ibid.
[7] Anna. Jour. Med. Research, 1912, xxix, 43.

mebæ. However, the work of Hartmann,[1] Whitmore,[2] and Walker,[3] as well as that of many other observers, has proven conclusively that these cultivated species are not true parasitic amebæ and should not be included in the genus *Endameba* or considered as identical with any of the endamebæ so far described as occurring in man.

The following species belonging to this genus have been identified as occurring in man:

Vahlkampfia lobospinosa Craig, 1912.[4]

Valkampfia withmorei Hartmann, 1912.[5] (This species was described by Maj. Whitmore, United States Army, and named after him by Hartmann, but the specific name is misspelled and should be "*whitmorei*." It is probable that the species is identical with *Valkampfia lobospinosa*.)

The only species actually identified as parasitic in man belonging to this genus is *Vahlkampfia lobospinosa*, an organism first described by Musgrave and Clegg[6] as ameba 11524. This ameba was cultivated by them from a dysenteric stool from a patient in Manila in 1905, and a culture was then sent to the Army Medical Museum, in Washington. I studied this species in cultures directly descended from the Musgrave culture, and in 1912 named it *Ameba lobospinosa*, emending the name in 1914 to *Vahlkampfia lobospinosa*. Other authors have described the occurrence of vahlkampfiæ in the stools of human beings and in the pus from liver abscesses, but the species concerned were not clearly identified.

While it is true that most of the species belonging to this genus are free living, it is also true that some species are apparently true parasites. This is proven in the case of *Vahlkampfia lacertæ*, a parasite of the intestine of lizards, while *Vahlkampfia mucicola* is ectoparasitic on fish and *Vahlkampfia pædophthora* is parasitic in the eggs and embryos of crabs. Several authorities have claimed that typical valkampfiæ are parasitic in in the intestine of man and may be demonstrated in both the vegetative and cystic stages of development in the feces, it being possible to observe the entire cycle of development in this locality. That this is undoubtedly true in some instances can not longer be denied, and I, myself, have had the opportunity of studying preparations sent me by Dr. W. M. James, of the Canal Zone, obtained from the feces of a patient at Panama, which contained both vegetative and cystic stages of a vahlkampfia which is indistinguishable morphologically from *Vahlkampfia lobospinosa*. This patient was observed for a considerable period of time and liability to accidental contamination of the feces was carefully guarded against. It is important to note that in these preparations the valkampfiæ present were perfectly typical in morphology of the same organism as observed in cultures and that they could be easily distinguished from true parasitic amebæ, as *Endameba coli* or *Endameba histolytica*. This observation is important because some investigators have endeavored to prove that, under certain conditions, as those present in the human intestine, valkampfiæ may so change in morphology as to be indistinguishable from, or perhaps identical with, the true parasitic amebæ or endamebæ.

The researches of Calkins and Williams,[7] who were the first to obtain *Vahlkampfia lobospinosa* in pure culture, have shown that upon certain special culture media this species forms trophozoites and cysts containing from four to eight or even more nuclei, whereas under normal conditions and on the usual culture media the trophozoites never contain more than two nuclei and the cysts are uninucleate. Owing to these very marked changes produced by environment, the authors mentioned warn against being too positive regarding the distinctive morphological and developmental features

[1] Anna. Jour. Med. Research, 1913, xxix, 43.
[2] Arch. f. Protistenk, 1911, xxiii, 71.
[3] Philippine Jour. Sci., sec. B., 1911, vi, 259.
[4] Archiv. Inter. Med., 1914, xiii, 737.
[5] M. Handbuch der Pathogenen Microorganismen, Kolle and Wassermann. Edit., 2, 1913, vii, 615.
[6] Musgrave, W .E., Bur. Govt. Lab. Biol., Manila, 1904, No. 18.
[7] Ibid.

claimed for the endamebæ of man, and suggest the possibility that there may be only one species of amebæ parasitic in the human intestine "manifesting different forms under different conditions," and indeed, Calkins[1] states that Williams has been successful in cultivating *Endameba coli*.

Now, the *Endameba coli* that Williams cultivated, as stated by Calkins, is Musgrave and Clegg's ameba No. 11524, or the same organism I have studied and named *Vahlkampfia lobospinosa*, a species, which when introduced into man, can be easily recovered from the feces in cultures and which, even after passage through the human intestine, retains the characteristic morphology of a typical vahlkampfia. Williams[2] definitely states that the ameba with which she worked is identical with my *Vahlkampfia lobospinosa* and as this species has been under cultivation since 1905 and the cysts resist drying for years (one year in my own experience and three years according to Williams), it is very evident that it can not be identical with either *Endameba coli* or *Endameba histolytica*, for the cysts of these species, as shown by several observers, notably Walker,[3] possess comparatively little resistance to drying. In addition while under the stimulating conditions present in certain culture media, this species does produce trophozoites and cysts containing several nuclei, the photomicrographs illustrating Calkins and Williams paper show conclusively that these multinucleate valkampfiæ are quite different in morphology from the endamebæ of the human intestine, the nuclear structure, upon which much stress is laid, being very dissimilar to that of either *Endamebe coli* or *Endameba histolytica*, in either the vegetative or cystic stages of development.

At the present time, while it must be admitted that certain species of *Vahlkampfia* may live a parasitic existence in man for a limited period of time, and while such species may be cultivated from the feces, there is no real evidence demonstrating that any of these species are pathogenic or that they can continue a parasitic mode of life indefinitely. The evidence of many investigators has proven that the vahlkampfiæ found in these rare instances of parasitic existence in man do not differ in morphology from those obtained from pond water or the air, the multinucleate cysts described by Calkins and Williams and the trophozoites containing more than two nuclei never having been observed in valkampfiæ obtained from the feces or other sources. The researches of these authors are most valuable in showing the enormous effect of environment upon the morphology and development of an ameba belonging to the genus *Vahlkampfia*, but they are far from demonstrating that this ameba is a true parasitic species or identical with any of the intestinal endamebæ of man.

In the vast majority of instances the valkampfiæ reach the feces or other material from which they may be cultivated by way of the air, as proven by Liston[4] and Wells,[5] or, in the case of the feces, by passing through the intestinal tract in contaminated food or water, and while certain species may, in rare instances, become parasitic for a short time in the human intestine, this is an abnormal mode of existence, no symptoms of disease are produced, and the organisms may be easily distinguished from the endamebæ of the human intestine by the large karyosome of the nucleus; the presence of at least one contractile vacuole; the uninucleate cyst; and by the fact that they can be cultivated upon artificial nutrient media, whereas there is no evidence demonstrating that any of the endamebæ of man can be so cultivated.

GENUS CRAIGIA CALKINS, 1912.

This genus was established by Calkins[6] in 1912, to include the ameba described by myself under the name *Parameba hominis*, in 1906.[7] I placed this parasite in the

[1] Musgrave, W. E., Bur. Govt. Lab. Biol., Manila, 1904, No. 18.
[2] Studies Research Laboratories, New York Board of Health, 1912, vi, 298.
[3] Philippine Jour. Sci., Sec. B, 1913, viii, 253.
[4] Quart. Jour. Micr. Sci., 1911, lvii, 279.
[5] Parasitology, 1911, iv, 304.
[6] Ibid.
[7] Craig, C. F., Am. Jour. Med. Sci., 1906, cxxxii, 214. Also The Parasitic Amebæ of Man. Phil., p. 215.

genus *Parameba* because of its resemblance to *Parameba eilhardi* Schaudinn, but Calkins rightly states that the fact that the flagellated stage of the parasite possesses only one flagellum, while *Parameba eilhardi* has two, is sufficient to throw it out of the genus *Parameba*, while he doubts if the accessory nuclear body described in *Parameba hominis* is identical with the Nebenkorper of *Parameba eilhardi*. On these grounds he considers that this parasite should be placed in a new genus, which he named *Craigia*. Calkins thus describes the characteristics of this genus:[1]

Small free-living or parasitic amebæ with a uniflagellated swarmer stage. Ameba stage from 10 to 25μ with little differentiation into ectoplasm and endoplasm when quiet, but with clear ectoplasm in movement. The endoplasm with or without an extranuclear body recalling the Nebenkorper of *Parameba*. The flagellated stage with a single flagellum.

Four species have so far been described as belonging to this genus, all of which are parasitic. Two species, which it is not necessary to describe here, are parasitic in marine worms, while two are parasitic in man. These are: *Craigia hominis* (*Parameba hominis*) Craig, 1906; emend Calkins, 1912; *Craigia migrans* Barlow, 1915.

Craigia hominis, the type species of the genus, was first noted by myself in the Philippines in the feces of patients suffering from a chronic form of diarrhoea and because treatment often resulted in the disappearance of the parasite and in the cessation of symptoms, I considered that it was probably the cause of the condition present.

The parasite is characterized by an amebic and flagellated stage of development. In the amebic stage the organisms measure from 10 to 25 μ while the flagellated forms are smaller (3 to 20μ). Endoplasm granular, containing a nucleus of a modified *limax* type and a small accessory nuclear body noted only in some of the larger parasites. Flagellated form spherical in shape and possessing a single flagellum. Multiplication of the flagellated forms occur by longitudinal division with division of the accessory nuclear body and motile organ. The amebic form encysts, the cyst having a double contoured membrane when fully developed. Reproduction in the amebic stage by simple division and in the cystic stage of the amebic form by swarmer formation within the cysts, the swarmers having a single flagellum. Habitat, human intestine where it causes a form of chronic diarrhea and dysentery.

More recently Barlow[2] has studied this parasite in Honduras where infections with it are quite frequently observed and has shown that it not only causes a form of chronic diarrhea, but also severe ulcerative conditions of the intestine resembling endamebic dysentery. He was able to study five infections in man with *Craigia hominis* and confirmed my own work concerning its morphology and cycle of development.

Craigia migrans, a new species, described by Barlow[3] and discovered by him at the time he was studying infections with *Craigia hominis*, in Honduras, is characterized as follows:

There is an amebic and flagellate stage of development. In the amebic stage the organisms measure from 12 to 30 μ, average about 20 μ; encysted stage measures about 18 μ. The young flagellates measure from 3 to 5 microns, and there are 40 or more in a cyst. Endoplasm granular and contains a nucleus but no accessory nuclear body. Flagellated forms are circular in shape and have a single flagellum. Multiplication of the amebic stage is by simple division and in the cysts by the formation of swarms, which are flagellated, and the cyst may contain from 20 to 40 of them. No multiplication occurs in the flagellate stage, the flagellate form, as soon as fully developed becoming an ameba. Habitat, the human intestine, where it produces severe dysenteric lesions and in some instances the liver is invaded and abscesses result.

Barlow studied 51 cases of infection with this parasite in man and demonstrated that it was the cause of a severe dysenteric condition of the lower bowel, sometimes accom-

[1] Craig, C. F., Am. Jour. Med. Sci., 1906, cxxxii, 214. Also The Parasitic Amebæ of Man. Phil., p. 215.
[2] Barlow, N., Am. Jour. Trop. Diseases and Prevent., Med., 1915, II, 680.
[3] Barlow, N., ibid.

panied by liver abscess. It will be noted that this species differs from *Craigia hominis* in that the flagellates become amebæ without multiplying as flagellates, and for this reason Barlow states that eventually it may be necessary to place this species in another genus.

Infections with both *Craigia hominis* and *Craigia migrans* are probably much more widespread and numerous than is generally supposed, owing to the liability of confusing these parasites with other amebæ or, during the flagellated stage of development, with cercomonads or trichomonads. In previous papers [1] I have considered in detail the differential diagnosis of *Craigia hominis* and the subject has also been treated of by Barlow in his excellent contribution, already quoted. It may be stated that a differential diagnosis between the parasites under discussion and other amebæ or flagellates may be made without much difficulty by attention to the differential characteristics of each organism outlined in these papers.

GENUS ENDAMEBA LEIDY, 1879.

The genus *Endameba*, which contains only parasitic species of amebæ, was established in 1879, by Joseph Leidy [2] who took for its type species *Endameba blattæ*, a parasitic ameba of the cockroach. In 1897, Casagrandi and Barbagallo [3] evidently in ignorance of Leidy's genus *Endameba*, established for the parasitic amebæ the genus *Entameba* and this spelling has been followed by the majority of protozoologists until quite recently. However, as there is no question of the priority of Leidy's work the proper designation for this genus is *Endameba* Leidy and not *Entameba* Casagrandi and Barbagallo.

The general characteristics of this genus may be outlined as follows:

Size comparatively small, from 5 to 80 microns. Ectoplasm and endoplasm distinct when organisms are moving and sometimes when motionless; ectoplasm clear and endoplasm either clear or finely granular, containing a nucleus which may or may not be visible in the living parasite; contractile vacuoles generally absent. Nucleus with or without a visible karyosome and centriole; reproduction by simple division, schizogony, and cyst formation with the production of several amebæ within the cyst. Habitat, the body of man or other animals, generally in the digestive tract. Some of the species are commensal while others are pathogenic. None have been artificially cultivated.

In this genus have been placed a large number of species that have been demonstrated to be parasitic in man and other animals but at the present time it is believed that many of the species described are not entitled to specific rank and for this reason our knowledge as to their exact classification is in a very unsatisfactory condition. No less than 26 distinct species have been described as parasitic in man, and these species are named in the following list, but as many of them have been determined to be identical with previously described species, I have so indicated after the specific name. For convenience of reference the list is arranged alphabetically:

LIST OF ENDAMEBÆ DESCRIBED AS PARASITIC IN MAN AND OTHER ANIMALS.

Endameba africana; Hartmann, 1907; identical with *Endameba histolytica;* host, man.

E. blattæ, Leidy, 1879; host, cockroach.

E. aulastomi, Noller, 1912; host, eagle.

E. bovis, Liebetanz, 1905; host, cattle.

E. braziliensis, Baurepaire Aragao, 1912; host, man.

E. buccalis., von Prowazek, 1907; identical with *Endameba gingivalis;* host, man.

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[1] Craig, C. F., Am. Jour. Med. Sci., 1906, cxxxii, 214; Archiv. Inter. Med., 1910, vi, I; Ibid., 1914, xiii, 737.

[2] Leidy, J., Rep. U. S. Geol. Surv., 1879, xii, I.

[3] P. Boll. d. Accad. Gioenia di nat. sc. in Catalonia., N. S., 1895, xxxix, 4.

E. butschlii, von Prowazek, 1912; host, man.
E. cobayæ, Walker, 1908; host, guinea pig.
E. coli, Loesch, emend Schaudinn, 1903; host, man.
E. confusa, Craig, 1916; host, man.
E. dentalis, Braun, 1883; identical with *E. gingivalis;* host, man.
E. duboscqi, Mathias, 1913; emend Craig, 1913; host, monkey.
E. dysenteriæ, Councilman and Lafleur, emend Craig, 1905; identical with *E. histolytica;* host, man.
E. gingivalis, Gros, 1849, emend v. Prowazek, 1907; host, man.
E. hartmanni, v. Prowazek, 1912; host, man.
E. histolytica, Schaudinn, 1903, emend Walker, 1911; host, man.
E. intestinalis, Walker, 1908; host, cat.
E. kartulisi, Doflein, 1901; host, man.
E. lacertæ, Hartmann, 1907; identical with *Vahlkampfia lacertæ;* host, lizard.
E. lagopidis, Fantham, 1910; host, moor-hen.
E. legeri, Mathias, 1913, emend Craig, 1914; host, monkey.
E. maxillaris, Kartulis, 1906; identical with *E. kartulisi;* host, man.
E. minuta, Elmassian, 1909; identical with *E. histolytica;* host, man.
E. miurai, Ijima, 1898; host, man.
E. mortinatalium, Smith and Weidman, 1910; host, man.
E. muris, Grassi, 1881; host, mouse and rat.
E. nipponica, Koidzumi, 1909; identical with *E. coli*, host, man.;
E. nuttalli, Castellani, 1908; host, monkey.
E. phagocytoides, Gauducheau, 1907; host, man.
E. pitheci, v. Prowazek, 1912; host, monkey.
E. polecki, v. Prowazek, 1912; host, swine and man.
E. pulmonalis, Artault, 1898; host, man.
E. ranerum, Grassi, 1879; host, frog.
E. salpæ, Alexeieff, 1912; host, fish.
E. schaudinni, Lesage, 1908; host, man.
E. suis, Hartmann, 1913; host, swine.
E. testudinis, Hartmann, 1910; host, turtle.
E. tetragena, Viereck, 1907; identical with *E. histolytica;* host, man.
E. tropicalis, Lesage, 1908; identical with *E. coli;* host, man.
E. undulans, Castellani, 1904; host, man.
E. urogenitalis, Baelz, 1883; host, man.
E. williamsi, v. Prowazek, 1911; host, man. Identical with *E. coli*.

Of the large number of species mentioned above it will be noted that about one-third have already been proven identical with previously described species, and it is more than probable that further research will demonstrate that the vast majority of the remainder are either mere variations of well known species or identical with them. As a matter of fact, there are only three species of endamebæ in the list that are of great interest to the physician—i. e., *Endameba coli*, *Endameba histolytica*, and *Endameba gingivalis*. These species have been well studied and their specific status demonstrated beyond any reasonable doubt.

Endameba coli, Loesch, 1875; emend Schaudinn, 1903. *Endameba coli* is a harmless commensal occurring in the intestine of a considerable proportion of healthy individuals in almost every part of the world. The species was first definitely separated from *Endameba histolytica*, the pathogenic endameba of the human intestine, by Schaudinn,[1] in 1903, and his observations were confirmed by Craig,[2] in 1905, and later by Hartmann,[3] Vedder,[4] Werner,[5] Whitmore,[6] and many others. Regarding

[1] Arb. a. d. K. Gesundhtsamte, 1903, xix, 547.
[2] American Med., 1905, ix, 854, 897, and 936.
[3] Arch. f. Protistenk, 1909, xviii, 207.
[4] Jour. Am. Med. Assoc., 1906, xxvi, 870.
[5] Indian Med. Gazette, 1909, xliv, 241.
[6] Ibid.

the occurrence of this species in health and in disease, its geographical distribution, and its life cycle and differential diagnosis from other endamebæ, the reader is referred to the papers just quoted.

Several other species have been described as harmless commensals of the human intestine, but it is more than probable that they are all identical with *Endameba coli*. This is certainly true of *Endameba tropicalis*, described by Le Sage;[1] *Endameba nipponica*, described by Koidzumi;[2] and *Endameba williamsi*, described by v. Prowazek.[3]

At the present time it may be stated that *Endameba coli* is the only species of endameba that has been actually demonstrated to be a harmless commensal in the human intestine.

The general characteristics of the species are as follows:

Size varies from 10 to 50 microns, the average being from 25 to 35 microns; ectoplasm and endoplasm only well differentiated when organism is in motion; movement sluggish and pseudopodia blunt; ectoplasm very slightly refractive; endoplasm finely granular, containing one to several noncontractile vacuoles. Nucleus well differentiated in the living parasite. Species not normally phagocytic for red blood corpuscles. Reproduction by simple division; schizogony, with the production of eight young amebæ; and by cyst formation, with the production within the cyst of from 8 to 16 amebæ, the normal number being eight. The cysts measure from 10 to 30 microns in diameter. Habitat, the human intestines, where it is a harmless commensal.

Endameba coli is of great practical importance to the physician in regions where endamebic dysentery occurs because of the liability of its confusion with *Endameba histolytica*, the cause of this form of dysentery, or with the amebic stage of *Craigia hominis* or *Craigia migrans*. As this species is found in the feces of a large proportion of healthy individuals, especially in the subtropics and Tropics, as well as in individuals suffering from diarrheal conditions not endamebic in origin, its differentiation from the parasites mentioned is essential before a diagnosis of endamebic dysentery or infection with craigiæ can be made, for if one were to rely only upon the presence of an endameba in the feces in the diagnosis of these infections without reference to the species present, it is evident that all infections with *Endameba coli* would be diagnosed as endamebic dysentery, and this is just what occurred prior to the differentiation of this species from *Endameba histolytica*. It has only been within a very recent period that care has been exercised in differentiating the actual species of endamebæ present in cases of suspected dysentery and even to-day this very important procedure is neglected by many clinicians.

The work of Walker and Sellards[4] has proven, through actual experimentation upon man, that *Endameba coli* is a harmless parasite, thus confirming the results of the animal experiments of Craig,[5] Strong and Musgrave,[6] and others, so that it follows that any diagnosis of dysentery of supposed endamebic origin based only upon the presence of an endameba in the stools is worthless unless the species of endameba present is ascertained.

Endameba histolytica Schaudinn, 1903; emend Walker, 1911. *Endameba histolytica* is the proven cause of a severe form of dysentery prevalent in both temperate and tropical regions, but especially so in the subtropics and tropics. The species was first clearly differentiated from the harmless *Endameba coli* by Schaudinn,[7] in 1903, although it had undoubtedly been described in part by almost every investigator of this form of dysentery, especially by Kartulis,[8] Councilman and Lafleur,[9] Strong and Musgrave,[10] and Craig.[11] However, Schaudinn was the first to place the species

[1] Ann. Inst. Pasteur, 1905, xviii, 9.
[2] Centralbl. f. Bakt., 1909, I, Orig., li, 650.
[3] Archiv. f. Protistenk, 1911, xxii, 345.
[4] Philippine Jour. Sci., Sec. B, 1913, viii, 253.
[5] Ibid.
[6] Annual Rep. Surg. General, U. S. Army, 1900, p. 251.
[7] Ibid.
[8] Virchow's Archiv. f. path Anat., 1886, cx. 521.
[9] J. Hopkins Hosp. Rep., 1891, v., p. 393.
[10] Ibid.
[11] American Med., 1905, ix, 864, 897, 936.

upon a firm basis, and although some of his interpretations of the morphology of the parasite were erroneous, his work has been confirmed by practically every student of the endamebæ of man.

An element of confusion arose with the description of a supposed new species of pathogenic endameba, the so-called *Endameba tetragena*, first described by Viereck [1] and afterwards accepted as a distinct species by most students of the subject. However, the recent researches of Walker,[2] Hartmann,[3] Whitmore,[4] James, [5] Darling, [6] and Craig [7] have proven that *Endameba tetragena* is merely a stage in the life cycle of *Endameba histolytica;* a stage erroneously described by Schaudinn and others, and first correctly described by Viereck in his description of *Endameba tetragena.* Therefore, it follows that the name *tetragena* has no longer value as the name of a species and can only be correctly used to designate one stage in the development of *Endameba histolytica.*

Since the differentiation of *Endameba histolytica* as a distinct species certain authorities have described other endamoebae occurring in diarrheal conditions and which they have regarded as new species, but all that have been carefully studied have been proven to be identical with *Endameba histolytica.* The most important of these so-called species is *Endameba minuta,* described by Elmassian [8] as a cause of dysentery in certain localities in South America, but recent work has proven that this species is really only a stage in the life cycle of *Endameba histolytica,* the so-called minuta stage, in which the trophozoites and cysts are smaller than those observed at other times.

The general characteristics of *Endameba histolytica* may be briefly stated as follows:

Size varies from 15 to 80 microns, the average being from 25 to 40 microns in diameter; ectoplasm and endoplasm well differentiated when organism is moving and frequently when motionless; ectoplasm very refractive and glass-like in appearance. Movement active and pseudopodia well developed, blunt or finger-like in shape. Endoplasm finely or coarsely granular, containing noncontractile vacuoles and a well-defined nucleus when the symptoms of dysentery are subacute, while if the symptoms are acute the nucleus is generally invisible in the living specimen. Normally actively phagocytic for red blood corpuscles. The nucleus varies markedly in appearance in stained specimens at different stages of development. Reproduction occurs by simple division; schizogony, with the production of four daughter amebæ; and cyst formation, with the production within the cyst of four amebæ. The cysts measure from 10 to 20 microns in diameter, the average being about 12 microns. They contain in addition to from one to four nuclei, characteristic chromidial bodies. Habitat, the intestine of man, where it produces the symptoms and lesions characteristic of endamoebic dysentery.

This species of endamobæ is the most important parasite belonging to the Rhizopoda so far as the medical profession is concerned, as it has been definitely proven to be the cause of that form of dysentery known as amebic or endamebic dysentery, a disease endemic in many parts of the world and which may occur in widespread and fatal epidemics when conditions are favorable. Thus the recognition of the parasite is of great practical importance as the early diagnosis of infection with it as almost essential if treatment is to be successful. Many very excellent descriptions of this parasite have been published by the authors already mentioned, and to their writings the reader is referred for a discussion of the morphology, life cycle, and differential diagnosis of this interesting and important species.

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[1] Archiv. f. Schiffs-u. Tropen-Hyg., 1907, xi, Beiheet I, 1-41.
[2] Philippines Jour. Sci., Sec. B., 1911, vi, 259.
[3] Ibid.
[4] Am. Jour. Trop. Dis. and Prevent. Med., 1913, i, 197.
[5] Ann. Trop. Med. and Hyg., 1914, Ser. T. M., viii, 133.
[6] Archiv. Int. Med., 1913, ii, 495.
[7] Jour. Infec. Diseases, 1913, xiii, p. 23.
[8] Elmassian, G. Centralb. f. Bakt., etc., 1909, I, Orig., 52, 335.

It may be stated here, however, that *Endameba histolytica* is peculiar in that at different stages of its development the morphology of the parasite varies so markedly that one might easily suppose that two species were being observed and it was this fact that lead the best authorities for so long to regard one stage in its development as a distanct species, which was named *Endameba tetragena*.

The relation of *Endameba histolytica* to dysentery has been quite recently proven beyond doubt by Walker and Sellards [1] by experimental work upon man, and while all of the essential points in their work had been perviously proven by experiments upon susceptible lower animals, their results possess the advantage of having been secured upon man, the natural host of this parasite. These investigators performed twenty feeding experiments upon as many healty individuals, using faeces containing cysts of *Endameba histolytica*, and of these eighteen afterwards showed the endamebæ in their faeces, and of these, four or 22.2 per cent had developed typical endamebic dysentery at the time of the publication of their paper.

Endameba gingivalis Gros, 1849; emend v Prowazek, 1907. This species of endameba occurs frequently in both the healthy and diseased human mouth, especially around the teeth, and the recent attempts that have been made to prove that it is the etiological factor in pyorrhea alveolaris have made it a species of considerable interest to physicians and dentists. It was undoubtedly first described by Gros,[2] in 1849, who named it *Amebia gengivalis*, and afterwards studied by Steinberg [3] and Grassi.[4] In 1904 v. Prowazek[5] gave a detailed description of the species under the name *Endameba buccalis* but as there is no doubt that the endameba described by the latter author is idential with *Endameba gengivalis* the name "*buccalis*" should be dropped as a specific name for this parasite.

Size varies from 7 to 35 microns, the average diameter being from 12 to 20 microns; ectoplasm and endoplasm well developed, the ectoplasm being visible only when motility is present. The ectoplasm is quite refractive and movement is quite active, the pseudopodia being well developed and short and blunt or long and fingerlike in shape. The endoplasm is granular, contains very numerous food vacuoles, noncontractile, but in the living specimen a distinct nucleus is not visible in most instances. The organism is actively phagocyic and red blood corpuscles are often ingested. Reproduction apparently occurs only by simple division during the vegetative stage of development. Cysts are formed containing one nucleus, but no reproductive changes have been observed within these cysts and it is probable that encystment in this species is a purely protective phenomenon. The cysts measure from 8 to 10 microns in diameter although larger cysts have been observed. Habitat, the human mouth.

There is no question that *Endameba gingivalis* is a distinct and valid species, although some authorities have endeavored to prove that it is identical with *Endameba histolytica*. However, the differences in morphology; the fact that the cysts formed by this species never contain more than one nucleus, the four nucleated cyst of *Endameba histolytica* having never been observed; and the absolutely negative results of all attempts to produce dysentery in susceptible animals by feeding experiments, prove that *Endameba gingivalis* is not identical with *Endameba histolytica*.

As regards the relation of this parasite to the etiology of pyorrhea alveolaris it may be stated that, at the present time, most authorities consider that it is not the cause of this condition. While the parasite is generally present around the teeth and in the abscesses of the disease, it also occurs in a large proportion of perfectly healthy mouths and there has never been the least proof adduced of an experimental nature connecting *Endameba gingivalis* with the production of pyorrhea. While it is at present impossible to absolutely deny that it may produce the disease, it is certainly

[1] Ibid.
[2] Bull. Soc. imp. de nat. de Moscow, 1849, xxii, 549.
[3] Souremenaya meditsina, Kiev, 1862.
[4] Gas. med Ital-Lomb., 1879, xxxix, 446.
[5] Arb. a. d. Kaiserl. Gesundhtsamte, 1904, xxi, 42.

true that we have no experimental evidence that it does, and the recent work of both physicians and dentists who have studied the subject is amply sufficient to lead us to conclude that this species of endameba is not the etiological factor in pyorrhea alveolaris.

The CHAIRMAN. We shall go on to the next paper and start our discussion after Prof. H. S. Jennings, of Johns Hopkins University, has read his paper on the "Origin of diverse races in difflugia corona."[1]

I would like to ask Dr. Jennings in regard to the method of reproduction of these difflugia. Was it invariably by the so-called budding division, Dr. Jennings?

Dr. JENNINGS. Yes, Dr. Calkins, and this is one of the questions on which I should like to get data. I have examined it as thoroughly and as far as I was able. I have not been able to find any actual observation of any other form of modification. The study of a single individual for nine months with respect to its method of reproduction seems a pretty fair test of whether the other form of reproducing itself occurred, because if a young individual does appear on your slide you can always tell if it is an individual that does not belong there. You can tell whether it is a contamination or not, by the fact that the tail gets pink-red as it gets old; and there was absolutely no appearance of an individual which could not be accounted for by simple fission, division, whatever you might call it.

The CHAIRMAN. I am still tempted to ask a question, and that is in regard to the chromatidiæ. Have you studied them, Doctor?

Dr. JENNINGS. I have not studied them. As you know, it is not possible to do everything. I think it very possible that the dissimilar formation that happens in chromatidiæ may very well have something to do with this.

The CHAIRMAN. It seems to me from what I have been able to gather as you went along that there is a possibility that this formation comes with the dissimilar development of chromatidiae which are here the bearers of hereditary characteristics. If there is no further discussion, we will pass to the next paper. Dr. Kofoid, of the University of California has sent his paper which will be read by Dr. Metcalf.

THE BIOLOGICAL AND MEDICAL SIGNIFICANCE OF THE INTESTINAL FLAGELLATES.

By CHARLES ATWOOD KOFOID,

Professor of Zoology, University of California.

A. INTRODUCTION.

The growth of interest in the flagellata in recent years has been stimulated in no small degree by the discovery of the relation of trypanosomes to disease, and by the

[1] At the author's request this paper is omitted from the Proceedings. The complete investigation has been published with details and illustrations, in Genetics, vol 1, pp. 407–534, September, 1916.

steadily increasing number of instances of parasitism by members of this group in the organs and tissues of both vertebrates and invertebrates with occasional instances of pathogenic consequences to the host.

In the field of comparative cytology this group has of late yielded data of prime interest to the problems of the evolution of nuclear and extranuclear structures of the cell, and of mitosis, to the nature and behavior of chromosomes, and to the fundamental problems of the organization of the living substance.

To this group we look for the first evidences of and most primitive phases of sexual reproduction, for the dawn of maturation phenomena, for the emergence of gametes and their sexual differentiation, and for the unfolding of the life cycle, but we have as yet, except in the volvocidæ, which are hardly typical flagellata, little evidence which can be regarded as final that true sexual reproduction occurs at all among flagellates.

It is the purpose of this paper to review recent advances in this field and to assess their value and significance in relation to current conceptions as to the distribution and parasitism of flagellates, to the organization of the flagellate cell, to the life history of flagellates, and to the processes of reproduction in the group, as well as to point out certain relations of these processes to the interrelations of host and parasite and to disease.

In data cited in this paper I make abundant use of results, some as yet unpublished, of investigations carried on under my direction in our laboratory at the University of California. I am especially indebted to Misses Christiansen and McCulloch and Drs. Swezy and Wilson upon whose work I draw freely as indicated in the bibliography.

B. OCCURRENCE OF PARASITIC FLAGELLATES.

The flagellata as a group surpass all other protozoa in numbers of individuals and range of environments successfully occupied. They outnumber the rhizopoda and ciliata in most habitats, and vie with the sporozoa in numbers in the cavities and tissues of their hosts. They range from the red snows of the polar regions and Alpine summits to the ooze of the ocean's depths. They swarm in all seas to the remotest shores, occur both in permanent lakes and rivers and in temporary puddles, and even in interstices of the soil. They abound in decaying organic matter and play a large part in the transformations attendant upon putrefaction and decay. They run the whole gamut of nutrition from the strictly holophytic dependence upon sunlight and inorganic materials, through the saprophytic or saprozoic, to the parasitic and pathogenic end of the series. As parasites they infest the majority of species of animals and some plants, and enter most organs and tissues, even to the innermost recesses of man's brain.

This great adaptability of the flagellate stock to a wide range of environmental conditions opens the door to a large development of parasitic forms, to complicated and irregular life cycles, to interchange of hosts, to transfer to new hosts, and to the causation of disease. It lends itself, in many forms, to a degree of variability within the species unsurpassed among other organisms. We have found, for example, that *Trichomonas augusta* from the intestine of amphibians lives and multiplies for some time in sterilized enriched tap water and in culture slides for many months quite apart from its normal host. Within an individual host it will sometimes show a very wide range of variation in size and proportions at comparable phases of the life history. It likewise passes through not only the flagellate stage, but becomes amoeboid, encysts, and loses its flagella.

C. PARASITISM AMONG FLAGELLATES.

The transition from the saprozoic mode of life to that of a parasite in the intestine of an insect or a vertebrate, and vice versa, is evidently easily made by some flagellates as is shown by the present existence of both free living and of parasitic species

in the same genus, as for example in *Hexamitus* and *Bodo*, and by the ease with which some at least (*Trichomonas augusta*) of the intestinal flagellates of the lower vertebrates live under saprozoic conditions in mixed pure cultures. These conditions thus favor the polyphyletic origin of the flagellates found as parasites and accordingly we find species or genera (which are parasitic) in most of the groups of flagellates, as for example in the protomonadina (*Trypanosoma*, *Bodo*), in the polymastigina (*Trichomonas*, *Hexamitus*, *Giardia*), in the euglenoidina (*Copromonas*), and in the dinoflagellata (*Blastodinium*).

The extent of the occurrence of flagellates as parasites among animals, especially in the invertebrates, is as yet very imperfectly known. There are indications that careful search will reveal their presence in most, if not all, species in which there is a well-developed digestive tract. The probability of the continual entrance of living flagellates into the digestive tract with food and water is apparent to anyone at all familiar with the microfauna of natural waters, and even of some distilled and bottled waters, as well as of the more favorable nidus provided in vegetable and other foods in which the initial stages of decay or putrefaction appear. The wonder is not that there are intestinal flagellates, but rather that there are not more of them.

The frequency with which they may be found is illustrated by the fact that in the course of the examination of 329 vertebrate hosts, most were found to be infected with one or more species of flagellates. Less than 2 per cent failed to yield flagellates from the digestive tract. Amphibia, 5 species, reptilia, 4 species, and mammalia, 6 species, were included as shown in the accompanying list.

List of hosts examined for flagellata.

AMPHIBIA.	
Diemyctylus torosus	25
Rana boylei	13
Rana draytoni	24
Rana pipiens	20
Hyla regilla	18
Total amphibia	100
REPTILIA.	
Eutenia sirtalis	2
Pituophis catenifer	5
Crotalus oregonus	1
Python reticulatus	4
Total reptilia	12
MAMMALIA.	
Belgian hare	12
Culture mice, gray and white	98
Culture rats, gray and white	42
Peromyscus maniculatus gambeli	59
Microtus californicus californicus	4
Canis ochropus ochropus	2
Total mammalia	217
Grand total of all hosts	329

The variety of the flagellate intestinal fauna which is harbored by a single host species is illustrated by the results of our examinations of 25 individuals of *Die-*

myctylus torosus. In this host species we found no less than 10 genera and 14 species of flagellates. The last two species named were probably derived from the alimentary canal of insects in which they are normally parasitic and are not digested with their host by the salamander.

PARASITIC FLAGELLATES FROM DIGESTIVE TRACT OF DIEMYCTYLUS TOROSUS.

1. *Trichomonas augusta* Alexeieff.
2. *Trichomonas batrachorum* Perty.
3. *Trichomonas* sp.
4. *Tetratrichomonas prowazeki* Alexeieff.
5. *Trichomitus parvus* Swezy.
6. *Hexamitus intestinalis* Duj.
7. *Hexamitus batrachorum* Swezy.
8. *Hexamitus* sp.
9. *Chilomastix mesnili* Alexeieff.
10. *Eutrichomastix* sp.
11. *Polymastix bufonis* (Dobell).
12. *Prowazekia lacertae* (Grassi).
13. *Monocercomonas melolonthae* (Grassi).
14. *Rhizomastix gracilis* Alexeieff.

D. EFFECT OF PARASITIC ENVIRONMENT UPON THE STRUCTURE OF THE PARASITIC FLAGELLATE.

In two very important particulars the flagellate living as a parasite is in an utterly different environment from that of its free living relatives and forbears. In the first place, it is subjected to new and different chemical conditions created by the digestive juices, the enzymes, and by the antitoxins produced by its host, some of them in response to its own chemical defenses and accentuated by its presence. These are biochemical products, and as such have a unique and peculiar facility in gaining access to the innermost structures and substances which enter into the organization of the flagellate. That they impose new adaptations of function and structure upon successful parasites is a reasonable hypothesis. It is also to be expected that these activities will manifest themselves, in part at least, in the increased functioning of the nucleus of the parasite in the production of extranuclear substances, hence the occurrence among parasitic forms of diverse chromidia and extranuclear chromatoidal substances, occurring as deeply staining clouds about the nucleus or of chromatin extrusions therefrom of unusual frequency and dimensions.

The second new and potent feature in the environment of the parasitic flagellate is the denser or more viscous medium in which its body is constantly bathed in the blood or lymph of its host or in its digestive secretions and digesting food. This feature of its surroundings involves at once an increase in the neuromotor organs and in the expenditure of energy, and this, in turn, accelerates the metabolism and activity of the chemical machine formed by the nucleus and cytoplasm.

Structurally it results in increase in the number and length of the flagella, in their differentiation into undulating membrane and axostyle, and in increasing complexity of their intracytoplasmic parts, as for example in *Giardia*.

Functionally it leads to movement on the substrate, to the extensive development of ameboid activities, and to the successful penetration of the epithelial palisade and other defenses of the host.

The extent to which the parasitic habit affects life history is as yet too little known even to speculate thereon. Suffice to say that there is evidence that the battle between host and parasite profoundly affects the nature and rapidity of multiplicative processes and favors cyst formation.

A recognition of the potency of these environmental factors in the evolution of the structure and life history of the flagellates will, in the opinion of the writer, tend to clarify our morphological interpretations of flagellate structure and to give a unity to the rapidly increasing revelations of their diversity. The failure to recognize these factors has, I believe, led us far astray in the prevalent conceptions of the extranuclear organelles, especially in the case of the so-called kinetonucleus.

B. THE MORPHOLOGICAL AND PHYSIOLOGICAL SIGNIFICANCE OF THE SO-CALLED "KINETONUCLEUS."

The distinction in many flagellates of two types of nuclei, the kinetonucleus and the trophonucleus, was first made by Schaudinn (1904) and Woodcock (1906) and has been widely adopted in the subsequent literature. It has led to the establishment of the order of protozoa, known as the binucleata, by Hartmann (1907) and the adoption of this system of classification in the bibliographies of protozoology published by Field in the Archiv für Protistenkunde. It has also given rise, or at least has lent support, to the binuclearity hypothesis as variously elaborated by Hartmann (1907, 1911) and others. This conception of the nuclear organization of the flagellate has thus been far-reaching in its influence on protozoological terminology and ideas.

This view was founded in large part on the now no longer accepted life history of *Trypanosoma*, described by Schaudinn (1904), in which its so-called ookinete gives rise by a heteropole mitotic division of its fertilization nucleus to a large central nucleus and a smaller one designated by Schaudinn as the blepharoplast. Woodcock (1906) later designated these as trophonucleus and kinetonucleus, respectively. According to Schaudinn the latter nucleus by a second mitotic division gives rise to the basal granule from which the flagellum grows out. The kinetonucleus thus arises as do other nuclei, by mitotic descent from a preexisting nucleus.

The interpretation presented in this paper of this so-called kinetonucleus is wholly different and has a fundamental significance in that, if true, it sweeps away the basis for the group binucleata of Hartmann, and also the grounds, in part, upon which the binuclearity hypothesis rests.

Without attempting in this connection to review the extensive literature pertaining to this subject, I will pass at once to the presentation of a different interpretation, based on functional considerations. The main thesis of this is that the locomotor activities of the flagellate type accentuated in parasitic forms by the increased expenditure of energy demanded of them by life in a denser, more viscous medium than that of their free-living relatives, have resulted in the development of an extra nuclear neuromotor apparatus of more than usual complexity, with a kinetic reservoir, the parabasal body. This is morphologically associated with the division center or centrosome consisting typically of a chromatic blepharoplast, usually containing the division center (or at least connected with it by a rhizoplast) from which the flagella are formed by outgrowth, and an adjacent structure of chromatic substance, the parabasal body, which is a sort of reservoir of substances used in the kinetic activity of the motor organelles in the viscous medium in which the parasite lives.

The neuromotor apparatus in nonparasitic flagellates usually lacks this parabasal body. It is not, however, everywhere absent—for example, Bělař (1915) describes in *Rhynchomonas nasuta* from the scum on stagnant swamp water, grown in cultures on amoeba agar of Hartmann, structures which lend themselves to the interpretation above outlined though not so interpreted by him.

The parabasal is lacking in some of his figures and the possibility that the structure we interpret as parabasal is a daughter blepharoplast is open. If not, it is probable that it disappears during mitosis. The point that we are making is that this apparatus is excessively developed in the parasitic flagellates and but slightly, if at all, in free-living ones.

I. Neuromotor Apparatus in the Protomonadina.

1. Prowazekia lacertæ (Grassi).

A simple and very instructive phase of its evolution is found in one of the simpler protomonadina, *Prowazekia lacertæ* (Grassi) from *Diemyctylus torosus*. In this form the blepharoplast at the base of the two flagella varies greatly in size, form, and evidently also in activity. It may be large and spheroidal, surrounded by a chromatic halo, or spreading in a fan-shaped suspensory rhizoplast passing toward the parabasal body. It is often connected with the nucleus by a slender rhizoplast.

The several phases of the parabasal body in this organism and the accompanying changes in the blepharoplast and nucleus are possibly instructive as indicating their interrelations and the method of origin of the parabasal. In stages in which the nucleus and blepharoplast both contain a large quantity of chromatin or deeply staining material, no parabasal can be found. In others, apparently premitotic stages, the central karyosome is replaced by numerous peripheral granules, and coincidently the blepharoplast is surrounded by a zone or halo of stainable substance. In other stages the rhizoplast is spread out in a fan-shaped structure running toward the nucleus and the parabasal body, and small masses of the stainable material are to be seen on its fibrous strands at various levels. The interesting feature of the parabasal is that it has various shapes, forms, and locations, suggestive of a highly metabolic condition. Moreover, the nucleus and blepharoplast are often poor in chromatin when the parabasal has its maximum size and vice versa. Our data are too incomplete to give a clear picture of the process, but as far as they go they suggest the origin of the parabasal at the expense of the chromatin of the nucleus the movement of stainable substance on the rhizoplast either to or from the blepharoplast at the base of the flagella and the wax and wane of the parabasal.

There is in this fluctuation in occurrence and structure of the parabasal of *Prowazekia* a striking resemblance to the form and behavior of mitochondria of the cells of the Metazoa (see Lewis and Lewis, 1915). The fan-shaped expansion of the rhizoplast also recalls the similar structure above the "kinetonucleus" of *Crithidia* and *Trypanosoma*.

A feature of prime significance in the life-history of *Prowazekia* is the fact that the parabasal divides at mitosis by constriction merely, without the slightest trace of a mitotic phase of its own.

2. Crithidia and Trypanosoma.

The nucleus and extranuclear structures of *Trypanosoma* are so well known that no separate discussion of them will be undertaken here beyond calling attention to the fact that no evidence of a satisfactory nature has ever confirmed Schaudinn's (1904) account of the origin of the "kinetonucleus" by mitosis from any nucleus by heteropole or any other type of mitotic behavior. In their recent exhaustive account of the life history of *Trypanosoma lewisi* Minchin and Thompson (1915) give no data whatever which can in any way be construed as justifying the use of the term mitotic to describe the divisions of the so-called "kinetonucleus."

The close relationship of *Crithidia* (*Herpetomonas*, *Leptomonas*) with the trypanosomes has long been evident. It is placed beyond all question by the discovery of *Schizotrypanum cruzi* by Chagas (1909) and especially by the full life history of *Trypanosoma lewisi* as worked out by Minchin and Thompson (1915) in the rat flea. In fuller confirmation of the close relationship stands the recently published outline of the life history of *Crithidia leptocoridis* from the box-elder bug, an herbivorous hemipteran insect, by McCulloch (1915).

The conditions are such that is is extremely probable that the whole life history of this parasite is passed within the digestive tract of this insect which feeds upon plant juices. Step for step, the life history and morphology of *Crithidia leptocoridis*

and of *Trypanosoma lewisi* up to the trypaniform phase are strikingly similar. At no time in the life history of either does the "kinetonucleus" either divide by mitosis or originate from the nucleus by any heteropole mitotic division. On the other hand, there is some very significant evidence that this so-called "kinetonucleus" is in reality a true parabasal body.

These organisms show an extranuclear chromatic mass, the parabasal body or so-called "kinetonucleus," from which the flagellum proceeds anteriorly along the margin of the undulating membrane. In many individuals in preparations there runs posteriorly, apparently directly through this "kinetonucleus," a chromatic thread, the rhizoplast, to the nucleus and sometimes to its karyosome. From the nucleus or from the blepharoplast at the base of the flagellum above the nucleus there runs posteriorly a slender chromatic thread which we provisionally call the axostyle, terminating near the posterior end in a chromatic granule. This appears to lie in or near the periphery but differs somewhat from the adjacent myoneme in size and undulations. This structure probably furnishes the mechanism for the posterior migration of the "kinetonucleus" in the trypaniform phases of the trypanosomidæ.

Let us now consider more particularly the morphological relations of this so-called "kinetonucleus." In the first place it lies posterior to the blepharoplast which is at the base of the flagellum; secondly, it is connected with this blepharoplast by a fan-shaped mass of suspensory fibers which might be designated as the parabasal rhizoplast; and thirdly, its appearance in the chromatic axis running posteriorly from the blepharoplast to the nucleus in many preparations and figures is more apparent than real. In reality it lies to one side of this line. A study of the figures of *Crithidia leptocoridis* (McCulloch, 1915) reveals the fact that this triangular ilol ed "kinetonucleus" lies in a great variety of positions with respect to the nuclear rhizoplast as though pendant from the blepharoplast and assuming various positions before the observer with the movements of the body and in its different aspects in the preparations.

These facts indicate that the "kinetonucleus" of *Crithidia leptocoridis* bears the same relations to the blepharoplast and rhizoplast as does the parabasal body of the polymastigina, as, for example, that of *Polymastix bufonis*. These considerations lead us to conclude that the "kinetonucleus" of *Crithidia* is the homologue in position and structure of the parabasal body of the polymastigina. It should therefore be called the parabasal body.

No indications of its origin by heteropole mitosis of any nucleus nor of its mitotic behavior at binary fission have been found. It rather seems to be connected with the blepharoplast and thence with the karyosome, and at spore formation (McCulloch, 1915), to come into intimate relations with it. Its emergence from the spore has not been followed.

At binary fission in *Crithidia leptocoridis* (McCulloch, 1915), it appears to divide by constriction as also in the case of *Schizotrypanum cruzi* (Chagas, 1909) and in *Trypanosoma lewisi* (Minchin and Thompson, 1915). There is no evidence that it undergoes mitotic division, or passes through any phase which justifies the assignment to it of nuclear attributes or the name kinetonucleus with the accompanying morphological connotation of the word nucleus.

The similarity of the structure of *Crithidia leptocoridis* to the crithidial stages of *Schizotrypanum cruzi* and to those of *Trypanosoma lewisi* gives presumptive evidence that the so-called "kinetonucleus" of the trypanosomidæ generally is in reality the parabasal body.

Confirmatory evidence of this is found in a new species, *Trypanosoma triatomæ*, Kofoid and McCulloch (1916) found by us in *Triatoma protracta* Uhler, a reduviid bug found in the nests of the wood rat, *Neotoma fuscipes macrotus* Thomas. The digestive tract of the bug often contains blood. We have not as yet been able to

examine the blood of the wood rat for trypanosomes. Presumably the flagellate parasite which is found in the digestive tract of the bug, in which it passes through both crithidial and trypaniform stages with remarkable similarity to *Schizotrypanum cruzi* in its invertebrate host, is in its trypanosome stage to be sought in the blood of the wood rat.

This flagellate which is an undoubted *Trypanosoma* in its developmental stages as far as known in the bug, we have demonstrated to have the same lateral attachment of the so-called "kinetonucleus" to the blepharoplast as in *Crithidia leptocoridis*, and the same fan-shaped suspensory structure spreading from the blepharoplast.

The morphological considerations set forth as a result of our examination of *Crithidia leptocoridis*, a trypanosomid flagellate which, so far as known, occurs only in the intestine of *Leptocoris*, a hemipteran insect, and of *Trypanosoma triatomæ* in both its crithidial and trypaniform phases in the hemipteran host *Triatoma*, lead us to conclude that the so-called "kinetonucleus" of these organisms is the homologue of that in the trypanosomidæ generally, and that it is laterally attached to the blepharoplast, a granule at the base of the flagellum, from which a rhizoplast is often found passing to the central karyosome of the nucleus and an axostyle passing toward the posterior end of the body. The striking morphological similarity of this type of structure to that found in the simpler polymastigina will be apparent when we come to consider the organization of that group. We hold that the "kinetonucleus" is accordingly in reality the parabasal body.

II. Neuromotor Apparatus of the Polymastigina.

In the polymastigina the neuromotor apparatus attains a much higher stage of complexity than in the protomonadina. This is seen in the increase in the number of the flagella, in the development of a powerful intracytoplasmic axostyle, in the various specializations of the parabasal, and in the integrating structures of the diplozoic hexamitidæ.

1. Polymastix bufonis (Dobell).

The simplest condition is to be seen in one of the lower polymastigina, *Polymastix bufonis* (Dobell) from the intestine of amphibians which has four very long equal anterior flagella, a fairly rigid body, a chromatic blepharoplast from which the flagella spring, located constantly at the extreme anterior end. This organ is also the division center, leading in mitosis but not taking a polar position on the intranuclear spindle on which polar caps replace the usual centrosome. From it two rhizoplasts pass centrally, one to the chromatin-poor spheroidal nucleus, the other to the chromatin-rich parabasal body, which forms a curved, club-shaped, deeply stained mass extending posteriorly to the nucleus.

The most instructive features of this parabasal body are its variable form, size, and position, its connection (often apparently lacking) with the blepharoplast, its diminution during mitosis, and its division by simple constriction, without mitotic activities on its part.

2. Trichomonas augusta Alexeieff.

The lateral detachment or inclusion of one flagellum to form the undulating membrane, the axial inclusion of another to form the powerful locomotor axostyle, and the almost continuous union of centrosome with the blepharoplast, is characteristic of many of the trichomonidæ (see Kofoid and Swezy, 1915, b). *Trichomonas augusta* Alexeieff, a parasite of amphibians, serves to illustrate this type, which for purposes of description may be regarded as typical of the higher polymastigina. In these trichomonad flagellates we find an apparatus which, when the cytoplasm is removed by maceration, remains intact. It consists of a series of structures radiating from the blepharoplast which is attached to the nuclear membrane by a

slender strand of stainable material, the rhizoplast. From the blepharoplast there radiate not only this rhizoplast, but also (1) the three anterior flagella; (2) an intracytoplasmic, laterally attached, posteriorly directed flagellum forming the marginal filament of the undulating membrane and projecting posteriorly as the posterior flagellum; (3) the axostyle, a swollen axial intracytoplasmic flagellum forming a powerful motor organelle used in locomotion on the substrate; (4) the parabasal body, or kinetic reservoir, a slender chromatic rod lying in the base of the undulating membrane, but not locomotor in function; and (5) the paradesmose which joins the polar blepharoplasts-centrosomes at mitosis and lies outside of the nuclear membrane. The blepharoplast which contains the centrosome initiates the process of mitosis. The division of organelles as well as their formation by new outgrowths alike proceed from it. The centrosomes may leave the daughter blepharoplasts with which flagella, paradesmose, and parabasal retain their connections, while it remains at the poles of the spindle. This separation, however, appears to be temporary in this organism but a permanent one in *Giardia* (*Lamblia*) *muris*. The permanent extranuclear location of the blepharoplast and centrosome in flagellates is suggested by the fact that the paradesmose is always extranuclear.

3. GIARDIA MURIS (GRASSI).

A more highly specialized phase in the evolution of this neuromotor apparatus is to be found in *Giardia muris*, a parasite of *Mus* and *Peromyscus* (see Kofoid and Christiansen, 1915, a, b). This is a binucleate somatella which might be regarded as made up of two individuals of *Trichomonas* retaining a single axostyle, which organelle, by the way, is the last to divide in the mitosis of *Trichomonas* and the first to divide in *Giardia*. The permanent condition of the trophozoite of *Giardia* is thus that of a *Trichomonas*, which has completed all of the steps in mitosis except division of the axostyle and plasmotomy. The early phases of mitosis in *Giardia* have given rise in the previous literature to the belief that *Giardia* has typically two axostyles.

The neuromotor apparatus of *Giardia* is even more definitely connected with the nucleus than *Trichomonas*. In nearly all individuals a chromatic rhizoplast runs from the blepharoplast to one pole of the elongated nucleus, expands on the nuclear membrane into a centrosome (*cent.*) and continues as an intranuclear rhizoplast into the central karyosome. The connections of the blepharoplast with the flagella, axostyle, and parabasals, are less distinct than in *Trichomonas*, owing to the crowding of structures about the head of the axostyle. From or near the blepharoplast on the head of the axostyle there arise in addition to the rhizoplast, (1) a chromatic commissure joining the right and left blepharoplasts; (2) the antero-lateral flagellum which apparently crosses over to the opposite side, runs along the cytostome posteriorly, and emerges at a lateral basal granule, and forms in the median line a node, the anterior chiasma at the point where it crosses its mate from the other blepharoplast; (3) the posterolateral flagellum which runs an intracytoplasmic course to near the margin of the body where it emerges without a basal granule; (4) the free ventral flagellum; (5) the axostyle attached to both blepharoplasts prior to the early phase of binary fission of the somatella; and (6) the dorsally located rhizoplast which runs to the parabasal body. There are two parabasal bodies, sometimes partially fused into one which are subject to considerable variation in size. They tend to disappear at mitosis, in both binary and multiple fission, and are entirely absent in encysting stages when locomotor activities cease.

In the light of the structure of the extranuclear organelles of both the protomonadina and the polymastigina we hold in conclusion that the parabasal body of the latter and the so-called "kinetonucleus" of the former are homologous organs, that there is no valid evidence for the derivation of this organ in either group by a heteropole or any other type of mitosis from any nucleus, and equally none for its division at binary fission by any process to which the adjective mitotic can be applied. In other words,

there are absolutely no morphological sanctions for the name kinetonucleus for this extranuclear chromatic structure. It is rather a chromatic extranuclear kinetic reservoir, and the noncommittal morphological designation "parabasal body" should be applied to it throughout, or the functional term "kinetic reservoir." The term kinetic or division center is wholly inapplicable, since the centrosome, or polar caps, or centrioles, are never contained within it, but rather in the blepharoplast or occur separately from both blepharoplast and parabasal, though with connecting rhizoplast as in *Giardia*.

III. Origin of the Extranuclear Neuromotor Apparatus.

The term neuromotor apparatus is used by us here and elsewhere to designate those organs of the protozoan body which carry on its coordinated motor and locomotor activities. They form a structurally continuous unit as shown in *Trichomonas* and *Giardia* connected by a rhizoplast with the nucleus as in *Trichomonas*, or with the central karyosome as in *Giardia*. On maceration of the cytoplasm in *Trichomonas* and *Trichomitus* this apparatus remains structurally intact for some time. It includes in *Trichomonas* the following structures: The anterior flagella, marginal filament of the undulating membrane, posterior flagellum, axostyle, parabasal body, blepharoplast, and rhizoplast. In *Giardia* there are added the anterolateral, postero-lateral, and free ventral flagella and an axostyle terminating in the posterior flagella the intracytoplasmic parts of the first two pairs of flagella just named, a rhizoplast going from the parabasal body presumably to the blepharoplast, and a cross commissure joining the right and left blepharoplasts. The integration of these parts in one coherent structural system and its intimate relation to the mobile cytostome are evident on an inspection of the figure. The repeated instances of the attachment of the blepharoplast to the nuclear membrane by a rhizoplast in the various flagellates which we have discussed and the direct connection of the neuromotor apparatus with the karyosome of the nucleus in *Giardia* give presumptive evidence of a fundamental structural and functional relation between the nucleus and this complex of extranuclear organelles. The fact also that the blepharoplast and its outgrowths and connections are basophile and stain more or less deeply with iron haemotoxylin suggests affinities if not similarities, of a chemical nature.

Added ground for regarding the extranuclear neuromotor apparatus as related to the nucleus and as evolved and derived from it is to be found in the results of Dr. C. W. Wilson's (1916) study of the life history of a soil amoeba *Naegleria gruberi*. This amoeba enflagellates on the impact of various environmental factors such as access of oxygen, or of fresh culture medium, and exflagellates with equal facility. In the amoeboid phase there is no extranuclear blepharoplast rhizoplast or flagella, and no chromatic extranuclear organelles, though chromidial formations are abundant and varied at times in the life history. As enflagellation approaches a chromatic process grows out from the central karyosome of the nucleus forming an intranuclear rhizoplast extending to the nuclear membrane. A granule appears at its tip and as this process continues its growth peripherally through the cytoplasm, retains its terminal position until it reaches the surface where it forms the blepharoplast connected on the one hand with the nucleus and on the other giving rise to the two flagella. In exflagellation the flagella shorten and fusing with the blepharoplast and rhizoplast appear to retreat again into the nucleus. In this connection we note the fact that no instances of mitosis were discovered in the flagellate phase, though they are to be expected, and in consequence we do not know the behavior of these organelles in that process. The centrosome or centriole is contained within the karyosome and appears here as in other amoebas at mitosis, at the ends of an axial chromatic thread in the center of the nuclear spindle. Thus in this amoeba the centrosome within the central karyosome of the nucleus originates the extranuclear neuromotor apparatus of the flagellate stage.

F. The Life Cycle of Intestinal Flagellates.

The life cycle of the protozoan, as for example, of *Paramecium*, is comparable in some of its aspects to that of the metazoan. It starts with the zygote or united gametes. There follows a period of binary fission in the protozoan, or of cleavage in the metazoan. Some, at least, of the resulting products in the protozoa become gametocytes, as do some of the cells of the metazoa. There is as yet no critical evidence to determine whether or not all individuals in the line of descent are potential gametocytes in the protozoa, or whether only a part of them are, as in the metazoa. The gametocytes in both protozoa and metazoa undergo a maturation process in which the chromosomes are reduced from the diploid to the haploid number with the resulting formation of gametes.

When we seek to apply this general formula to the data at present available as to the life history of intestinal flagellates and, indeed, of flagellates generally, excluding the phytomonadina, we find a serious lack of conclusive proof as to the occurrence in them of this life cycle as above outlined. Asexual reproduction is well known, although, as we shall shortly show, one important phase, that of multiple fission, has been largely overlooked and sometimes denied. Sexual reproduction, on the other hand, is less clearly established among flagellates than in any other group of protozoa.

I. The Sexual Phase.

The occurrence of periodic or occasional sexual reproduction among the parasitic flagellates is to be expected on a priori grounds. It has long been known among the phytomonadina in *Volvox* and has recently been demonstrated by Chatton (1911) in *Pleodorina californica*. Among other groups of flagellates Dobell (1908) has given an account of a sexual cycle in *Copromonas subtilis* (*Euglenoidina*) from the frog, and Goldschmidt (1907) has elaborated a very full description of a sexual cycle in the free-living rhizomastigina in two genera, *Mastigella* and *Mastigina*, of rhizopod affinities with a cycle of the rhizopod type. The process of autogamy, described by Prowazek (1904) and others, and rather widely accepted, we believe to be, in part at least, erroneous, being founded on the inclusion of a yeast, *Blastocystis* (Alexeieff, 1911) in the life cycle of the flagellate. This process is in need of confirmation.

The difficulties in the way of tracing the sexual cycle are great. Multiple infection by different parasites opens the door to confusion of different species in one life cycle, a pitfall which trapped even the far-sighted Schaudinn. Involution phenomena, especially nuclear extrusions of chromatin, simulate maturation phenomena. The occurrence of stainable products in the cytoplasm in uniting (or dividing?) flagellates such as Dobell (1908) figures for *Copromonas* is hardly to be regarded as a conclusive proof that maturation has taken place. Amoeboid activities of the still attached sister cells at the close of mitosis but before plasmotomy in binary fission afford, in fixed preparations, most, if not all, of the stages necessary to build up an account of the fusion of gametes, except that of nuclear fusion. After one has followed the protean changes of such a living couple he approaches the subject of sexual reproduction and especially of fertilization stages with a very vivid sense of the difficulty of securing from anything but the living gametes in the actual process of sexual behavior and from fusing gametic pronuclei any conclusive evidence of sexual reproduction among flagellates without morphologically distinguishable gametes.

Another uncertainty of considerable import arises from our lack of knowledge regarding the nature and function of encystment, and the condition or conditions which induce it. We have as yet no clear evidence that this process is in these flagellates necessarily related in any way to sexual reproduction, though stages suggestive of it are found in the so-called "copulation cysts" of *Giardia*, which contain two binucleate individuals in a definite morphological position one to the other; that is, end to end, and back to back. Supplemental to this is the discovery in *Giardia microti* (see Kofoid and Christiansen, 1915 b) of such cysts in which the formation of reduc-

tion nuclei is at least simulated. These may be only involution phases, with degenerating normal nuclei. The difficulties in the way of considering these true copulation cysts are great. These "gametocytes" are binucleate. This does not preclude the formation of uninucleate gametes, but no traces of such a condition have appeared in our material. There is no evidence of reduction in the number of chromosomes in these nuclei under suspicion as reduction nuclei by reason of their size and appearance in "copulation cysts."

On the negative side attention must be called to the failure of prolonged and intensive investigation on the life cycle of trypanosomes, such as that of Minchin and Thompson (1915) on *Trypanosoma lewisi*, in bringing to light the least evidence of the occurrence of a sexual phase in the invertebrate host, the flea. The discovery of the so-called sexual reproduction of *Trypanosoma* by Prowazek (1905) in the louse, is as yet without adequate confirmation. It rests also in the first instance on isolated occurrences in smear preparations of fixed material, of contiguous so-called anisogametes, and not on continued observation of the sexual behavior of living gametes and of the resulting zygote.

In out own observations (Kofoid and Swezy, 1915 b, and Kofoid and Christiansen, 1915 b) on the life history of four genera, *Trichomonas*, *Eutrichomastix*, *Tetratrichomonas*, and *Giardia*, and Dr. Swezy's observations (1915 a, b, and 1916) on *Hexamitus*, *Polymastix*, *Bodo*, and *Prowazekia*, no conclusive evidence of a sexual cycle has as yet been detected, when due caution is observed to avoid the pitfalls above enumerated. The sexual cycle is to be sought and is probably to be expected, but the evidence for it is to-day far from conclusive, and such as we have bears no comparison in its finality with that available in the case of the ciliata.

II. THE ASEXUAL PHASE.

This phase of the life cycle as we have found it is divisible into two distinct stages. (1) binary fission with mitosis followed by delayed plasmotomy and yielding two daughter trophozoites, and (2) multiple fission forming by three successive pervading mitoses an 8-zooid plasmodium or somatella, which by a process of disintegrative plasmotomy later gives rise to eight small or young trophozoites. In the binucleate flagellates such as *Giardia* and *Hexamitus* a 16-nucleate, but still 8-zooid plasmodium, is formed. There is no return in either binary or multiple fission in these forms to a uninucleate condition, at least in so far that at each succeeding mitosis the growing somatella is composed, not of 4, 8, and 16 separate and uniform cells, each of which ultimately, after disintegration of the temporary phase of union, forms a new individual, but rather of 2, 4, and 8 binucleate potential individuals united in a common cytoplasmic mass, but each fully equipped with the coordinating neuromotor organelles of the individual.

We have verified the occurrence of both of these processes of asexual reproduction in 12 species belonging to 6 genera. Both (except as noted) have been found in *Trichomonas augusta*, *T. muris* (Kofoid and Swezy, 1915 b), in *T. sp.*, and *T. batrachorum* (results not yet published), in *Eutrichomastix serpentis* and *Tetratrichomonas prowazeki* (Kofoid and Swezy, 1915 a, b), in *Hexamitus muris*, *H. intestinalis*, *H. ovatus*, and *H. batrachorum* (multiple fission only), in *Trichomitus parvus* (Swezy, 1915 a, c) and in *Chilomastix mesnili*. Binary fission alone has thus far been seen in *Polymastix bufonis* and *Prowazekia lacertæ*.

This widespread occurrence of these processes justifies in our opinion the expectation that both binary and multiple fission will prove to be normal phases of the life history of intestinal flagellates and probably of most flagellates. It will suffice for present purposes to note their occurrence in the protomonadina, in *Trypanosoma lewisi* as described by Minchin and Thompson (1915), and to briefly outline these processes in the polymastigina in three typical forms, *Polymastix bufonis* (Dobell), *Trichomonas augusta* Alexeieff. and *Giardia muris* (Grassi).

I. BINARY FISSION IN INTESTINAL FLAGELLATES.

This process in the polymastigina consists of two distinct phases: (1) Mitosis involving both nuclear and extranuclear structures, and (2) plasmotomy resulting in the separation of the daughter individuals. These two phases are far less intimately connected than in metazoan cells, and a considerable interval may elapse after the first is completed before the second ensues. Mitosis is of the promitotic type with the nuclear membrane remaining intact and is often, but not always, accompanied in the polymastigina by the formation of an extranuclear chromatic thread joining the sister blepharoplasts at the poles of the spindle, but lying wholly outside of the nuclear membrane. The extranuclear organelles are wont to initiate the mitotic process and to behave rather independently of the intranuclear phenomena. Within the nucleus an intranuclear chromidial cloud is succeeded by a skein stage from which twice as many chromatic rods (chromosomes) emerge as later appear in the equatorial plate, thus giving the appearance of a precocious splitting and subsequent fusion of these structures. It is also noteworthy that the chronology of mitotic phenomena in the dividing organism is subject to many variations with the result that a very considerable variety of pictures of the process may be obtained. This is to be expected in view of the parasitic mode of life and the peculiar susceptibility of mitotic phenomena to the subtile influence of biochemical factors. Let us now briefly consider binary fission in three types, *Polymastix bufonis* (Dobell), *Trichomonas augusta* Alexeieff, and *Giardia muris* Grassi.

(*a*) Binary fission in *Polymastix bufonis* (Dobell): The blepharoplast initiates binary fission by its division, each daughter taking two of the four flagella. No paradesmose is formed between them and they are at no time located at the poles of the spindle. The central karyosome disappears, an intranuclear chromidial cloud is formed, from which four chromosomes emerge, which fuse to form two in the equatorial plate. In the telophase these fuse with the chromatic polar caps. At the close of mitosis the parabasal body whose rhizoplast appears in one instance to be split, parts by simple constriction. Neither it nor the blepharoplast show at any time any features which might be properly designated as even remotely resembling the mitotic processes of the nucleus. Plasmotomy ensues progressively from the anterior end posteriorly; that is, the division is a longitudinal one.

(*b*) Binary fission in *Trichomonas augusta* Alexeieff: This has been described in full elsewhere (Kofoid and Swezy, 1915 a, b) so that a brief review only will be given here of its most salient features. It is initiated by the division of the blepharoplast and of the attached flagellum or chromatic margin of the undulating membrane, and by the outgrowth of one new flagellum. The intranuclear chromidial cloud emerges as a circumnuclear halo and later both cytoplasmic and axostylar chromidia increase in number. The central karyosome is succeeded by a chromatin skein and this in turn by the emergence of 10 or twice as many chromatin masses (chromosomes) as appear later in the equatorial plate. The chromosomes are differentiated as to size and behavior, there being a small one lagging in the anaphase. As the metaphase approaches, the daughter blepharoplasts migrate to the poles of the spindle, spinning out a deeply staining paradesmose between them which persists for a long time as a sort of tether between the daughter nuclei. It is always extranuclear. Each blepharoplast takes with it its quota of old and newly outgrowing flagella and its undulating membrane and parabasal, a new parabasal having been formed by outgrowth from the blepharoplast alongside the old. At the metaphase or amphiaster stage the polar blepharoplasts may be temporarily abandoned by the centrosomes which retain a polar position while all of the extranuclear neuromotor organelles, except the axostyle, retain their attachment to the blepharoplast.

With the migration to the poles of the daughter chromosomes the reorganization of the daughter nuclei is preceded by the equatorial constriction of the parent nucleus and their sudden rounding up and separation. This latter process is probably aided

by the motor activities of the reattached blepharoplast with its flagella which again fuses with the polar centrosome. The connection of the nuclei and blepharoplasts with the axostyle is apparently lost during this process and it is only in the latest stages of mitosis that this organ divides lengthwise, splitting from the anterior end posteriorly. We have not found that it disappears and is reformed from the paradesmose as Dobell (1909) and others have stated. The daughter nuclei become attached to the heads of the daughter axostyles and in this condition the organism remains for some time while undergoing protean changes in form as the two daughters struggle persistently and incessantly to sever the band which unites them. With the accomplishment of plasmotomy the process is completed.

(*c*) Binary fission in *Giardia muris* (Grassi): The process of binary fission in this organism is complicated by the fact that it is diplozoic and possesses an integrated neuromotor apparatus. We have elsewhere described this process in detail (see Kofoid and Christiansen, 1915 b) and will review it briefly here. The normal trophozoite contains but a single axostyle. Previous accounts of its structure showing two axostyles may rest on early stages of mitosis.

Mitosis is initiated in *Giardia* by the division of the blepharoplasts and is followed at once by that of the axostyle which splits longitudinally from the anterior end posteriorly. The centrosome on the anterior end of the nucleus divides and one daughter moves to the opposite pole, spinning out an extranuclear chromatic paradesmose. Division of the anterolateral flagellum progresses distally from the blepharoplast to the anterior chiasma.

In the meantime an intranuclear chromidial cloud has been replaced by a split skein and this in turn by an equatorial plate with four chromosomes in two groups which constrict at their middle and the daughters migrate to the poles. Nuclear constriction parts the daughter nuclei. During mitosis the parabasals disappear and reappear later in the daughter organisms.

Plasmotomy is a slow process during which the daughter zooids assume many different positions with respect to one another. Before they finally part each is fully equipped with a complete set of organelles and phases of an ensuing mitosis may even appear, though these may be indications of an impending multiple mitosis.

In closing this brief discussion of binary fission and mitosis attention is called to two main points; (1) the elaborate system of extranuclear neuromotor organelles intimately connected with karyosome and centrosome, and with a more or less evanescent and variable parabasal or kinetic reservoir, and (2) that there is no second nucleus or other structure to which the term kinetonucleus can be applied by reason of origin, structure, or function. There is no mitotic continuity of origin, no content of chromosomes, no mitotic behavior on the part of any extranuclear structure in either the protomonadina (*Trypanosoma*), or in the polymastigina (*Trichomonas*) of sufficient validity, backed by indisputable evidence, to justify the further continuance of the term kinetonucleus in protozoan terminology. There is now in hand a sufficient body of criticism on the one hand, and of constructive evidence on the other, to seriously raise the question if it is not in the interests of sound protozoological progress to rid ourselves of the conception of nuclear dualism as applied to the flagellata with its resultant consequences in our ideas, terminology, and classification.

2. MULTIPLE FISSION IN INTESTINAL FLAGELLATES.

There has been heretofore much doubt (see Jollos, 1913, Alexeieff, 1914, Prowazek and Werner, 1914) as to the occurrence of this phenomenan among intestinal flagellates. We have, however, demonstrated its prevalence (see Kofoid and Swezy, 1915 b and Kofoid and Christiansen, 1915 b) among a number of genera and species. Its importance as a feature of the life cycle is thus established but its significance with respect to sexual reproduction, if it has any, is as yet problematical. It is not accompanied by any reduction in the number of chromosomes as will appear on an inspec-

tion of our figures (Kofoid and Swezy, 1915 b) of the process in *Eutrichomastix serpentis* in which there are four chromosomes throughout both binary and multiple fission in all of its stages through the 8-nucleate plasmodium. Possible importance of the occurrence of this phase in intestinal flagellates in their relations to their hosts is suggested by the parallel with the malarial parasite, but there is here no cytoplasmic residuum after multiple fission to release endotoxins as in *Plasmodium*. We will now briefly describe this process in intestinal flagellates.

(*a*) Multiple fission in protomonadina: It has been definitely established that it occurs in the crithidial phase of *Trypanosoma lewisi* within the cells of the stomach wall of the flea (Minchin and Thompson, 1915). There is a probability that it also occurs in the cells of the wall of the midgut of *Leptocoris trivittatus* in the case of the minute phases of *Crithidia leptocoridis* (see McCulloch, 1915) and in the intestinal cells of *Euryophthalmus convivus* in the life history of *Crithidia euryophthalmi* (McCulloch manuscript, 1916), but the details of the process are inadequately known. There are, however, sufficient indications to justify the expectation that further search for this phase among the protomonadina will be rewarded.

(*b*) Multiple fission in the polymastigina: (1) *Trichomonas augusta* Alexeieff. This has been described by us elsewhere (Kofoid and Swezy, 1915 b) in full, so that only a brief review of its essential features will be given here. It consists of three rapidly succeeding mitoses, with the accompanying formation of a complete set of new extranuclear neuromotor organelles accompanying each nucleus as in mitosis in binary fission, but without accompanying plasmotomy. This results in the successive formation of a 2, 4, and 8 nucleate plasmodium or somatella of amoeboid form and activity, provided, respectively, with 6, 12, and 24 flagella, and 2, 4, and 8 axostyles and undulating membranes, all capable of motor activity and vigorously lashing about.

This plasmodium or somatella then proceeds to disintegrate piecemeal by dropping a single zooid at a time, or at least not by the coincident separation of all the zooids. As will be seen in the figures the struggles of the individual zooid eventually free its sister and cousin zooids, but this process of disintegrative plasmotomy is a prolonged one.

(2) *Giardia muris* (Grassi). The process of multiple fission in this diplozoic organism, is not the formation of two groups of eight nuclei descended respectively from the right and left nucleus of the somatella, but the establishment of bifurcating 2, 4, and 8 zooid plasmodia by three succeeding pervading mitoses. In other words it is a plasmodium of zooids and not merely of cells. At each step of its formation the zooids appear to be quite fully equipped with the extranuclear neuromotor organelles, except the parabasals which disappear early in the process, and the chromatic border of the cytostome which is but partly developed in its anterior region only.

Multiple fission in the free stage in *Giardia* is followed by disintegrative plasmotomy apparently by the successive detachment of individual zooids. Multiple fission occurs not only in the free stage but also in cysts, in which case nuclear multiplication proceeds with no corresponding divisions of the extranuclear structures which more or less disappear. The fate of such cysts with 16 nuclei is as yet wholly unknown. There is no evidence of reduction of chromosomes in them.

G. The Biological Significance of the Life Cycle of Intestinal Flagellates.

The formation among flagellates of a definite plasmodium or somatella, as a regular, though somewhat brief phase of the life cycle, is prophetic of the organization of the more permanent multinucleate, also multicellular body of the metazoa. In all of these flagellates mitosis and plasmotomy are two distinct processes and the latter results from the ceaseless struggles of the component zooids of the common plasmodium which finally rend asunder the viscous plasma and thus complete the establishment of their separate individualities. The component zooids of this plasmodium have little or no structural or functional integration to bind them together and the disintegration of the somatella into its component units is only a question of time.

It is a matter of no small biological significance that the binucleate genera *Hexamitus* (*Octomitus*) and *Giardia* (=*Lamblia*) represent structurally an integrated pair of flagellates with the following structural evidence of such integration, bilateral symmetry, single ventral cytostome, single (not double, as heretofore described) axial axostyle, commissure joining the two blepharoplasts across the head of the axostyle, and a union in the median plane of the two antero-lateral flagella in the anterior chiasma, thus linking together the neuromotor apparatuses of the two component cells. Functional integration is seen in the locomotor behavior, in the parallel position and common stroke of the free ventral flagella of the two component cells, in the functioning of the ventral cytostome as a single sucker or organ of attachment, and in the motor activities of the single axostyle or of the paired daughter axostyles during mitosis.

From the evidence in hand it appears that in the hexamitidae we have a clear instance in which a multinucleate body in its lowest possible terms, to wit, a binucleate somatella, has been evolved from an already highly specialized ancestral flagellate by the structural and functional integration of its already complex structural features. The temporary binucleate somatella occurring in the interval between mitosis and plasmotomy in other flagellates has in *Hexamitus* and *Giardia* become the permanent condition of the organism. This union fails to become permanent in other flagellates, as does that of the eight zooids in the somatellæ of all flagellates, because of the absence in them all of the essential integrating structural basis, and the absence in these stages of the unified behavior of its component parts.

H. The Medical Significance of the Life Cycle of Intestinal Flagellates.

The relationships of these parasites to an absorbing surface, their intense locomotor activity on the mucus substrate of the intestinal epithelium, their tendency to creep into the crypts and their ability (*Giardia*) to traverse the intestinal palisade and enter the blood stream in the central lacuna of the villi, all mark them as probably more than mere harmless commensals. In cases of light infection and in perhaps 50 per cent of the hosts we have examined, our casual inspection has detected no evidence of lesions, or of intestinal modification by the parasite. In cases of heavy infection, however, there is indisputable evidence that they are associated with more or less breaking down or thinning out of the intestinal epithelium, even dropping off of the villi, and considerable local disintegration of the cells of the intestinal epithelium. Bacterial infection is heavy in such localities. Externally the region of infection can usually be detected, especially in the lower vertebrates, by the flaccidity of the wall, often accompanied by swelling of the intestine by the gelatinous material which is there localized in the lumen.

In mice an infection by *Giardia muris* is accompanied by a characteristic yellowish translucent color of the intestine which is brighter in tone than in cases of infection by *Trichomonas muris*, and the contents are more gelatinous and more viscid. These conditions are readily detected in heavy infections upon opening the abdominal cavity. There is considerable evidence that *Giardia* is far more pathogenic in its tendencies than are the other genera. It occurs as *G. agilis* in tadpoles, but not in frogs. *G. muris* is more abundant in young than in old mice. *G. lamblia* of man (=*Lamblia intestinalis*) is often reported from children. These facts suggest that juvenile infection imparts a degree of immunity to the adult.

Certain facts derived from wild mice in culture suggest, but as yet do not prove, that infection which is higher among culture mice may be a cause of a dwarfing of wild mice under cultural conditions. Other causes are operative here and their relative potency has not as yet been analyzed.

Two phases of the life cycle brought to light by our investigations have a possible bearing on the interrelations of host and intestinal flagellate parasites and sources of

pathogenicity of the latter. It is well known that the period of schizogony in the malarial parasite marks the climax of its biochemical assault upon its host. There is some very incomplete evidence that both binary and multiple fission in these intestinal flagellates is periodic, and pervading, though none that this periodicity is regular. Hosts in which either process occurs are relatively rare, and though mitosis may be found sparingly in many hosts there are some instances in our records in which it was exceedingly abundant in a given host.

Multiple fission in like manner is restricted to a few host individuals among the numerous ones examined by us. In the case of *Trichomonas augusta* these were found mainly in the months of July and August. These facts point toward the cyclic occurrence of these phenomena of reproduction among these parasites. A second phenomenon of interest in this connection is the occurrence at mitosis among these parasitic forms generally, of the intranuclear chromidial cloud followed, in some cases at least, as in *Trichomonas augusta*, by the increase in the number of extranuclear chromidia, and in the amount of extranuclear chromatin or deeply staining substance in the cytoplasm. Similar conditions attend the mitotic phases of multiple fission in this form. In some other flagellates, as in *Giardia* at the time of mitosis, the parabasal body fades away. There are thus indications that at the time of mitosis the metabolic processes of the organism involve an unusual activity on the part of the chromidial and extranuclear stainable substances of the cytoplasm. Moribund individuals with an unusual amount of such cytoplasmic inclusions occur in hosts in which binary or multiple fission is in progress. There is a possible basis here for a climax in the toxic effect of the parasite on its host at these periods of reproduction.

Still another feature of the action of the parasite upon its host is to be recognized in its ceaseless motor activities and in the tendencies for the fission stages, both binary and multiple, to creep about upon or into the intestinal epithelium. They become at these periods sources of stimulus or irritation to the epithelial cells and may possibly open lesions for the entrance of bacteria into the blood stream of their host. The enormous numbers of *Giardia* in the mammal and of *Crithidia* in hemiptera are such that with their habit of attachment to the intestinal cells they form a veritable living carpet on the walls of the infected region of the intestine.

The biological data regarding intestinal flagellates thus suggest that they are associated with conditions simulating chronic enteritis and that they may be sources, especially at reproductive phases, of ectotoxins, and on their death of endotoxins, and that they may be a source of irritation or of lesions by virtue of their motor activities. They can not all be regarded as merely harmless commensals.

I. Summary.

1. Parasitic flagellates have a wide distribution in the digestive tract of both vertebrate and invertebrate hosts. Many different species (14 in *Diemyctylus torosus*) may occur in a single host species, sometimes coincidently.

2. Most subdivisions of the flagellata have contributed to the parasitic faunas of animals, especially the protomonadina and polymastigina.

3. The conditions of parasitic life in a denser, more viscous medium increase the difficulties of locomotion, and have resulted in the evolution of additional motor organelles and the establishment of a highly differentiated, coordinated, neuromotor apparatus. They also cause a greater expenditure of energy, with accompanying increase in metabolism and development of extranuclear chromatic substances, especially the parabasal body, which is a reservoir of such substances closely related to the blepharoplast at the base of the flagella.

4. The doctrine of nuclear dualism in the protozoa advanced by Schaudinn, Woodcock, and Hartmann, which recognizes a trophonucleus and a kinetonucleus rests on an erroneous interpretation of this parabasal body in the trypanosomes and other

parasitic flagellates. The so-called kinetonucleus does not arise by heteropole mitotic division of a parent nucleus, does not contain chromosomes, does not divide by mitosis, but by simple splitting, constriction, or outgrowth, and in general has none of the attributes of a true nucleus except similar stainability with certain stains. It is in reality laterally attached to the blepharoplast at the base of the flagella and is morphologically and functionally the parabasal body or kinetic reservoir.

5. The binuclearity hypothesis is untenable as applied to the flagellates, the binucleata as a systematic concept should be abandoned, and the doctrine of nuclear dualism in the protozoa should be restricted to the ciliata.

6. The neuromotor apparatus is derived (in *Naegleria gruberi*) from the karyosome of the nucleus, centers in the blepharoplast, which usually, but not always, contains the cytoplasmic division center, and includes structures attached to, or growing out from the blepharoplast, such as flagella, axostyle, marginal filament of the undulating membrane, parabasal body, and rhizoplast. It is mainly basophile and chromatic.

7. The neuromotor apparatus is an integrated structure which in the diplozoic flagellates (*Giardia*, *Hexamitus*) forms a single structural and functional system uniting the motor organelles of the two cells in one structural unit.

8. Sexual reproduction among intestinal flagellates, and flagellates generally, except the volvocidæ (close to the metaphyta) and rhizomastigina (close to rhizopods) is, as yet, of doubtful occurrence. "Autogamous cysts" belong probably to a yeast (*Blastocystis*). "Copulation cysts" have not been proved to contain gametes. More critical investigation is needed here.

9. Asexual reproduction is of two types, (1) binary, and (2) multiple fission, both of wide occurrence among intestinal flagellates.

10. Binary fission involves mitosis and subsequent plasmotomy. Mitosis is of the promitotic type with nuclear membrane intact throughout the process. The blepharoplast may or may not contain the centrosomes permanently or temporarily. Definite chromosomes of constant number and differentiated form and behavior appear in the equatorial plate. Precocious splitting or doubling occurs after the nuclear skein, but the chromosomes reunite in the equatorial plate and pinch apart without evidence of any relation to the earlier plane of fusion.

11. The blepharoplasts form an extranuclear paradesmose between them. This does not form the new axostyles which do arise, however, by longitudinal splitting of the parent axostyle. The axostyle is a locomotor not a skeletal organ.

12. Plasmotomy is a slow process and results from the motor activity of the daughter zooids.

13. Multiple fission in intestinal flagellates (polymastigina) results from three pervading successive mitoses with the accompanying formation of the extranuclear neuromotor apparatus for each nucleus. It results in the successive formation of a 2, 4, and 8 nucleate plasmodium or somatella. In the diplozoic flagellates it forms a 4, 8, and 16 nucleate somatella, but these are primarily 2, 4, and 8 zooid somatellas, since each zooid is fully equipped at each stage (except in multiple fission in cysts) with the normal extranuclear organelles.

14. Plasmotomy is a slow process of progressive detachment of individual zooids from the common somatella which lacks integrating structures or coordinated behavior of its parts.

15. The formation and prolonged existence of the plasmodium or somatella among flagellates is significant as indicating a tendency to form a multinucleate body as in the metazoa. Such a body in its lowest possible terms, from the standpoint of cellular components, is seen in the two-celled diplozoic flagellates such as *Giardia*. These are evolved by the persistent union of the component cells of a 2-nucleate plasmodium and the development of an integrated neuromotor apparatus, and accompanying integrated behavior. It seems probable that the diplozoic organism is derived from the highly differentiated uninucleate type resembling *Trichomonas*.

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16. The intestinal flagellates are not all harmless commensals. Some of them accompany inflation of the intestine locally, the accumulation of a viscid yellowish gelatinous mass in the lumen, the thinning out and breaking down of the intestinal epithelium, and they may even create lesions and enter the blood stream.

17. Their mobility on the surface of the intestinal cells, their tendency to creep into the crypts and even into the wall itself creates a source of local stimulus or even of irritation.

18. Their cyclic reproductive processes with accompanying fluctuations in metabolic activity is indicated by varying amounts of chromatic materials in the cytoplasm and creates a basis for a climax in their biochemical relations to their hosts.

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The CHAIRMAN. Dr. Kofoid's paper furnishes a stimulating record of the life history of these parasites. The next paper on the program is that of Dr. C. H. T. Townsend.

DISCOVERY AND IDENTIFICATION OF THE STAGES IN THE ASEXUAL CYCLE OF THE CAUSATIVE ORGANISM OF PERUVIAN VERRUGA.

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For the benefit of those who may not be acquainted with the nature of the disease known as verruga, and in order that all present may properly understand the subject-matter of this communication, I will say that this disease, which is confined to certain deep and narrow valleys or canyons in the western face of the Andes in Peru, is believed by practically the entire Peruvian medical fraternity, who have made a very extensive study of the subject, to consist of four stages, in which belief I concur.

I. An incubative stage, without visible external symptoms.

II. A fever stage, with slight to marked rises of temperature, type intermittent or remittent, accompanied by more or less marked anemia, with more or less pronounced articulation, bone and rheumatoid pains, and more or less marked blood changes, during which certain bacilliform bodies occur in the red blood corpuscles and other stages of these bodies occur as vascular cell inclusions in the lymphatic nodes, spleen, and other organs.

III. A quiescent stage, without apparent external symptoms other than general bodily weakness.

IV. An eruptive stage, during which a more or less wartlike eruption, consisting very largely of vascular-cell proliferation, with more or less mononuclear infiltration, appears in the subcutaneous tissues and often in the internal organs, certain vascular cell inclusions occurring in the eruption tissues.

I should add that Dr. R. P. Strong, of Harvard medical school, and his associates have recently announced their firm conviction that the fever and eruptive stages just described are two distinct pathologic entities, or two separate and independent diseases; the fever, which they call *Oroya fever*, being specifically caused by the bodies found in the erythrocytes, lymphatic nodes, and other organs; the eruption, which they call *verruga peruviana*, being caused by a specific virus which they consider resident in the eruption tissues, presumably comprising ultramicroscopic organisms. The paper which I am about to present will, I believe, prove conclusively that such is not the case, but that the fever and eruption are phases or stages of one and the same disease.

I should also state that during 1913 and 1914 I carried out in Peru an investigation of the insect transmission of verruga. Without going into details, it is sufficient for our present purpose to say that I believe that I have fully demonstrated *Phlebotomus verrucarum*, a small and delicate bloodsucking gnat, the only strictly crepuscular and nocturnal bloodsucker confined to the infected zones, as the vector of verruga.

It is the purpose of the present communication to interpret correctly the stages in the asexual cycle of the causative organism of verruga from the findings already published, which, however, have been supplemented and verified by similar findings in my own material. The significance of these was first pointed out by me before the Biological Society of Washington on December 4, 1915. The published findings will be taken up in chronologic order.

In 1909 Dr. Albert L. Barton, of Lima, Peru, described as "x-bodies" the mature gamete stage of this organism, discovered by him in 1905 in the erythrocytes of the peripheral blood of verruga cases in the fever phase. Drs. Strong et al. have redescribed the same stage under the name *Bartonella bacilliformis*.

In 1911 Dr. S. T. Darling, then at Panama, figured gametes found by him in verruga blood smears from Peru, among which he gives a figure of an erythrocyte filled with minute rods which he termed "young x-bodies," and which will be referred to as Darling's x-bodies. These are the immature gametes of Bartonella, shortly after penetration of the erythrocyte.

In September, 1912, Drs. Gastiaburu and Rebagliati, of Lima, discovered certain "cuerpos" or bodies in verruga eruption tissue and in liver of verruga cases in the eruptive stage, which they figured and described as Leishmania-like. These are respectively early and maturing schizonts of Bartonella, before they have begun to break up into merozoites. Their figure of the eruption smear shows a cell containing many of the very early schizonts, while their figure of the liver smear shows maturing schizonts which are largely free.

In April, 1913, Drs. Mayer, Rocha-Lima, and Werner, of Hamburg, figured and described certain "Zelleinschluesse" or cell inclusions which they found in vascular endothelial cells of the greater part of the verruga nodules examined by them from a case of the disease just arrived from Peru. Their figures 1 to 4 show the cell inclusions entire, while 5 and 6 show them ruptured. These are evidently to be interpreted as respectively maturing Bartonella schizonts and Bartonella merozoites which have resulted from the breaking up of schizonts.

In 1915 Drs. Strong et al. figured and described certain "spheres" found by them in vascular endothelial cells of lymphatic nodes and spleen of verruga cases in that phase of the disease which they term *Oroya fever*. They state that these spheres apparently break up into a large number of minute elements each containing a chromatin granule, these becoming elongated and finally appearing as distinct rods containing at one end a minute particle of chromatin. The spheres shown in Strong's figures 1 and 2, plate X, are obviously an earlier stage of Mayer, Rocha-Lima, and Werner's cell inclusions, being early schizonts of Bartonella and in more or less nearly the same stage of development as Gastaiburu and Rebagliati's eruption smear bodies. Figure 3, plate X, corresponds to Mayer, Rocha-Lima, and Werner's figures 1 to 4, and

to Gastiaburu and Rebagliati's liver smear bodies, being the maturing schizonts of Bartonella. Figure 6, plate X, shows the merozoites of Bartonella largely in their early stage, before elongation. Figures 4, 5, and 7, plate X, show the elongated stage of the merozoites. Drs. Strong et al. state that the minute rodlike elements, or elongated merozoites, are identical in character with the gametes in the erythrocytes. After entering erythrocytes, and before completing their growth, they are evidently to be considered immature gametes, and are the same as Darling's x-bodies. The work of Drs. Strong et al. has thus resulted in establishing a definite connection between Barton's x-bodies, Darling's x-bodies, Gastiaburu and Rebagliati's cuerpos, and Mayer, Rocha-Lima, and Werner's Zelleinschluesse, which was hitherto not apparent. Drs. Strong et al., however, appear to have suspected no connection between their vascular cell bodies from the fever stage and those previously announced from the eruptive stage. I may add that I am able to identify these bodies in my own sections and smears of verruga.

The relationship existing between all of these bodies, and the correspondence of those of Drs. Strong et al. with the previously announced bodies, can be seen in the diagram. The conclusion is obvious that all are stages of the same organism, *Bartonella bacilliformis*. The schizogonic cycle of Bartonella in warm blood can be easily followed in these stages. We have only to assume the existence, in the salivary glands of *Phlebotomus verrucarum*, of the sporozoites, a stage as yet undetected by us but certainly existing by analogy with the life cycle of similar pathogenic organisms.

All of these findings indicate conclusively that Bartonella is a protozoan. Several facts, which are easily explained, have proved stumblingblocks, however, in the interpretation of the asexual development of the organism. It has been repeatedly demonstrated that blood containing mature gametes of Bartonella fails to originate any symptoms upon injection into healthy animals; that the gametes disappear from the erythrocytes upon the advent of the eruption; that it is impossible to grow these gametes in ordinary culture media; that eruption-tissue inoculations produce localized proliferation lesions in new tissues without gametes of Bartonella appearing in the erythrocytes; and that such lesions may be produced successively in series of animals by such inoculations. These and related facts are what induced Drs. Strong et al. to announce the fever and eruptive stages of verruga as two distinct pathologic entities. But their finding in Oroya fever cases of the schizonts and merozoites of Bartonella, already shown to be characteristic of the eruption tissues, appears to bind inseparably their *Oroya fever* and *verruga peruviana*. The explanation of the several facts above mentioned will appear below.

It is evident that the greater numbers of the Bartonella sporozoites introduced by the Phlebotomus within the skin of susceptible subjects immediately embed themselves in the cytoplasm of the vascular endothelial cells at points of inoculation. Once embedded, they develop into schizonts, which upon maturing break up into merozoites, the latter elongating within the unruptured host-cell walls and penetrating such erythrocytes as come into direct contact with the infected cell, whereupon they become immature gametes. The fully formed rods and ovals in the erythrocytes are respectively the mature male and female gametes, which can conjugate only in the Phlebotomus, or at least in cold blood. Hence their injection into a healthy warm-blooded animal fails to originate any symptoms of the disease. There appears to be no duplication or repetition of any of the stages, so far as the forms already found afford any index, except that the mature male gametes may increase by binary transverse division. But there is some reason to believe that the merozoites before elongation may under certain conditions develop into schizonts.

The endothelial cells of the capillaries of the subcutaneous tissues are evidently the chief seat of the above-described schizogonic or asexual cycle of Bartonella, and here is where the erythrocytes mostly become infected. The fever stage follows the extensive breaking up of the schizonts in the endothelial cells of the capillaries, and

its inception coincides with the extensive penetration of the erythrocytes by the merozoites. The toxin resulting from the multiplication of Bartonella has been liberated in quantity into the blood, causing the rise of temperature, the anemia following through hemolysis.

The eruption, which is particularly characterized by a great proliferation of vascular endothelial cells, is the direct result of the extensive asexual multiplication of Bartonella in the subcutaneous tissues. The proliferation of vascular endothelial cells, incited by the toxin resulting from the metabolism of Bartonella, not only imprisons this toxin, thus arresting the hemolysis, but also prevents the erythrocytes from coming into direct contact with cells containing merozoites, thus cutting short the infection of the erythrocytes. As the natural result the fever and anemia both subside, and the gametes of Bartonella are no longer to be found in the blood.

Erythrocytes can evidently become infected only during their slow passage through the capillaries and while in actual contact through positive chemotropism with a living infected endothelial cell in situ in the capillary wall. Evidently the infected cell is positively chemotropic for normal freshly-oxygenated erythrocytes, attracting and holding them in contact with itself until transfer of a certain number of merozoites has been effected, which decreases the oxygen tension in their substance, thereby transforming their tropic qualities, the sufficiently infected erythrocytes being set free through negative chemotropism. Hence eruption-tissue inoculations produce no gametes in the erythrocytes of the subject inoculated, for the merozoites contained in such material, enveloped as they are by masses of proliferation, are obviously unable to come in contact, under proper conditions, with the erythrocytes in the new tissues. Eruption-tissue inoculations are, in a sense, mere transplantations or grafts, as proved by the fact that the resultant proliferation is strictly localized. They are comparable not only in behavior, but also to a considerable degree in character, to the grafts of carcinoma and other tumors which have been effected within recent years.

The cause which leads to localized proliferation in new tissues following eruption-tissue inoculations appears to be purely physical in character. The new proliferation results from a specific chemophysical irritation of the endothelial cells in the capillaries of the new tissues by the proliferation substance introduced, and is not due to any new activity of a living organism. It is toxin-incited, not virus-incited. The original proliferation possesses a specific chemophysical reaction, inherited from the inciting toxin and transmissible within certain limits to the new proliferation which it induces. Such new proliferation may be successively repeated in verruga, within limits, by inoculation of old proliferated cells into new tissues. This explains the proliferation lesions obtained by Drs. Strong et al. in 12 successive series of monkeys, which lesions they consider due to a virus resident in the proliferated tissues used for inoculation. However, they were unable to obtain the lesions by injection of a filtrate from these tissues, the reason being that the proliferated cells can not pass the filter; they found that inoculation of these tissues upon the rabbit's cornea produces no lesion, the reason being that the cornea possesses no vascular cells; and their attempts to cultivate the supposed virus resulted in failure, the reason evidently being that no living virus in the common acceptation of the term exists in the proliferation tissues. They did succeed in determining the presence in the eruption tissues of a hemolysin which they state is active in relatively high dilutions. This is very much to the point. This hemolysin is quite certainly the toxic by-product of the reproductive activity of Bartonella in the subcutaneous tissues; is the specific cause of the anemia of the fever stage; and is the agent which directly incites the proliferation of the vascular cells, thus causing the eruption lesions. In other words, this toxin is able to destroy erythrocytes, to irritate vascular cells sufficiently to cause their proliferation, but has no effect on such dense connective-tissue cells as compose the cornea.

Some of the sporozoites introduced by the Phlebotomus within the skin must reach the lymphatic nodes, spleen, bone-marrow, and liver, as well as the capillaries of the

submucous tissues, carried thence by the lymphatic system on their failure to embed in the subcutaneous tissues, these unembedded sporozoites being picked up in the serous canaliculi. If this happens extensively, internal eruption results. This explains the infarction, necrosis, and other pathologic changes in the internal organs, as well as the articulation and bone pains, all so commonly noted in the disease, especially in the fever stage. In most cases the fever and visible eruption in verruga correspond very faithfully in intensity. When this correspondence is not so marked it is practically certain that infection of the internal organs has become proportionately greater, resulting in an increased internal eruption.

In conclusion, I would say that we are now, for the first time, getting some tangible evidence as to the etiology of verruga. Those familiar with the facts so far known relating to this unique disease will at once see how perfectly they all fit together, now that we interpret the cell inclusions of the eruption tissues as a part of the schizogonic cycle of Bartonella. Incidentally, the unity of verruga appears to be established by the known stages of its specific causative organism.

The CHAIRMAN. The discussion of these papers is now open.

Dr. TYZZER. There are certain points in these papers which I would like to comment upon. In the first place the inclusions which were described by Gastiaburú and Rebagliatri in the internal organs were described as leishmania. There was nothing in common between those and the inclusions which we found in the endothelial cells in Oroya fever. I do not see that there can be any connection between these inclusions as we are familiar with them. There were other inclusions found in verruga, which Rebagliatri demonstrated to us as clematozoa. Neither of those could be associated with the inclusions which we found in the endothelium in Oroya fever. I regard those observations of the organism in the endothelium as observations of a new body or stage. Of course, the organism in the corpuscle was observed by Barton and by Gastiaburú previously.

With regard to the basis for our differentiating two diseases, we studied the lesions of verruga Peruana at all stages. These tissues were taken from the human being and studied fresh by the dark field, in stained smears and stained sections. We have never found anything in the endothelium of a verruga nodule which can be interpreted as an organism or which is in any way similar to the findings in Oroya fever. I may say that our material is abundant and was collected under the best of conditions, and I think I have applied most of the valuable methods of technique. We inoculated monkeys, dogs, and rabbits, and also one human being. The inmate of an institution was inoculated with the verruga nodule, and this produced local lesions just as we had obtained in the animals. There was no Oroya fever which followed after inoculation. In the monkey we produced lesions which were carried on for successive generations; I have forgotten how many, but I should say it was 10 or 12 successive generations. That this can not be transplantation of tissue is shown by the work in transplantation of tumors with which I am quite familiar.

In transplantation of tumors it is quite out of the question to transplant tissues of one species to another species and have the tumor continue to grow for any length of time. I do not think that the transplantation of tissue can account for these lesions which are produced. We are firmly convinced that it is a disease, a transmissible disease, which is transmitted to monkeys by inoculation, and in the dog we had a few observations of lesions which corresponded with those of the human verruga lesions. By inoculating the testes of the rabbit in a manner similar to that in which syphilis is transmitted to the rabbit, we produced lesions here also. They were not of the same type as those found in the human lesion; they were more exudative, more inflammatory, and there was not a proliferation of the endothelial cells.

So I think we have here a fairly good basis for the differentiation of Oroya fever and verruga as two distinct diseases, and notwithstanding our abundant material we can not confirm the presence of these organisms in the lesions of verruga.

Dr. LUNG. Mr. Chairman, I have nothing to contribute to the technical knowledge of this subject, but I wish to call the attention of the meeting to a circumstance in connection with the study of this disease which, at the present time, has much significance. Twenty-seven years ago, in the course of my journeyings as a naval medical officer, I found myself in the harbor of Callao, and remained there for two months. Following the impulses of my youth and my professional instinct, I looked into the diseases that prevailed in this locality, and my attention was at once called to this disease, verruga. At that time, it was of great moment to certain commercial interests of Peru. They were just constructing a wonderful railway from the city of Lima to the top of the Andes, and in building this road they had encountered this disease. The conditions attending the building of the road had apparently increased the conditions which produce the disease, and men were made ill by the hundreds, incapacitated for work, and many died. The condition was a parallel to that prevailing in the building or the attempt to build the Panama Canal by the French. In consequence, this disease gave them great concern, and in the light of the knowledge we had of such diseases some study was made; and I, following the guidance of some medical officers, accumulated a good deal of information and made a report, published in the Surgeon General of the Navy's record the following year, that was of necessity immature and incomplete, a mere compilation of what was then known.

The point I wished to speak about particularly was this: In connection with the efforts of the medical men of our sister Republic, Peru, to determine what this disease was and what caused it, there was one young man who had not only the enthusiasm to pursue it

vigorously, but he inoculated himself with the exudate or one of the incrustations which appear at a certain stage of the disease, and in consequence contracted the disease and died. We love to think of some of the martyrs of our profession who have submitted to such procedures, some with very striking and good results. Here was a young man who lost his life. Unfortunately, he acquired no definite knowledge or imparted no knowledge to those who surrounded him. But at this particular time, when we are endeavoring to promote good feeling and professions of friendship with South America, we should bear in mind a man like Daniel Carrion, who was willing to give up his life to science. He has been made a martyr in his country, and due recognition has been given to him there.

The CHAIRMAN. Is there any further discussion?

Dr. LUNG. I want to ask a question, if I may. After being in Peru, I went to the Philippine Islands, and there I saw a disease known as parangi (yaws). The onset, the clinical course and the results, outwardly at least, are exactly similar to those of verruga. I would like to ask these gentlemen if they have made observations on this point. I believe some efforts have been made, but so far as I know nothing has been determined conclusively.

Dr. TOWNSEND. I can only say that Dr. Strong and his associates have demonstrated the distinctiveness of verruga peruviana and parangi (yaws). As to the remarks of Dr. Tyzzer, I do not wish to prolong the argument, but I simply stand on the arguments in my paper and would invite a careful comparison of the figures and descriptions of these cells.

Dr. GUITERAS. I would like to ask Dr. Townsend whether there has been any further experiment with the Phlebotomus verrucarum. As I understand it, there was one single experiment.

Dr. TOWNSEND. There are no experiments, I believe, except those I carried on, and I performed a good many on laboratory animals and one on man, and published the results of these. I used great quantities of phlebotomus in the different experiments, and I think that my published results will contain conclusive proof that Phlebotomus verrucarum is the vector of the disease.

Dr. GONZÁLEZ-RINCONES hereupon spoke in Spanish.

The CHAIRMAN. Dr. Guiteras, will you kindly translate the remarks of Dr. Rincones?

Dr. GUITERAS. Dr. Rincones has called attention to a case of a German who had gone through the Oroya Valley and afterwards came to Venezuela and there developed the disease, and he calls attention to the fact that they saw there in one man the two stages of the disease. They saw the fever stage and afterwards that of the eruption. Dr. Rincones says that they were not able to find the parasite

in the different stages that have been described. He finally calls attention to the fact that parangi (yaws) in the Philippine Islands is an entirely distinct disease, the microorganism of which is well known.

The CHAIRMAN. If there is no further discussion, we will proceed with the reading of the papers by Dr. L. E. Migone.

UN NUEVO FLAGELADO DE LAS PLANTAS (LEPTOMONAS ELMASSIANI).

Por LUIS E. MIGONE,

Profesor de Bacteriología de la Facultad de Medicina de Asunción, Paraguay.

En una excursión practicada el año pasado en los lugares pantanosos del Río Salado, desagüadero de la Laguna Ihpacaraí, no lejos de Asunción (Paraguay), con motivo de una epidemia de mal de caderas desarrollada en los carpinchos (*Hydrochœrus capivara* L.), recordando los estudios de Lafont sobre ciertas especies de Euforbías en la Isla Mauricio; los de Carrougeau y Lafont en Tamatave, Diego Suárez; los de Noc y Stevenel en las Antillas, me detuve a examinar el jugo o savia de las plantas que con verdadera exuberancia crecen en esas regiones. Una de ellas resulta interesante, una asclepiadasea: la *Araujia angustifolia* (Gris) que en la primavera (septiembre a diciembre) cubre con sus tenues ramas y espeso follaje los arbustos que le son próximos.

Examinando al microscopio el jugo lactescente de esta planta, con una buena lente de inmersión, se observa que las finas granulaciones emulsionadas en el líquido gomoso, están en continuo movimiento ondulatorio, comunicado por un ser completamente invisible por su trasparencia. Este movimiento puede durar en la preparación más de 24 horas. La extensión del latex sobre láminas, una buena fijación por el calor y una coloración lenta de 12 gotas de la solución colorante de Giemsa, en 30 gramos de agua destilada, durante 12 horas, nos demuestra perfectamente bien que, el movimiento vibratorio observado en el líquido, es efectivamente producido por seres organizados, semejantes a los encontrados por Lafont en las Euforbías.

Este microorganismo se encuentra en general en toda la planta y en todas las de la misma especie que habitan la región. Las pequeñas raíces, el tallo, las ramas juncosas, las hojas, cáliz de la flor, los verdes o maduros frutos, se encuentran invadidos por innumerables leptomonas.

En el invierno (junio a septiembre) cuando esta planta se encuentra reducida a su tronco y finos tallos, no desaparecen sus parásitos. Por lo general las curvaturas de las ramas y la corteza de la fruta contiene más parásito que en las demás partes.

Esta planta trasportada a otro lugar, a otro suelo, al de Asunción por ejemplo, a pesar de la facilidad con que se desarrolla, pierde paulatinamente sus parásitos. Lo mismo ocurre con las plantas nacidas de semilla, de plantas infectadas.

Las hojas y el tallo despiden un olor desagradable con el quebrantamiento y no he podido observar que ningún animal la apetezca. Ningún insecto vive sobre ella. El microorganismo es sumamente tenue y frágil. Los fijadores, en general, no le convienen; el alcohol parece disolver sus cromatinas; los fijadores de Zenker o Schaudinn, que requieren largos lavados consecutivos, tampoco me han proporcionado buenos éxitos para la coloración. Sólo el calor a cien grados sí presta gran ventaja sobre los líquidos fijadores. La solución colorante más conveniente es la de Giemsa como ya lo he dicho.

El cuerpo es finamente granulado, con la extremidad anterior terminada en punta roma y la posterior en una punta afilada en forma de cinta retorcida sobre sí. Presenta un grueso núcleo coloreado intensamente del básico; el centrosoma o blefaroblasto ocupa ya la parte media entre el núcleo y la extremidad anterior, o ya más hacia el

núcleo. Una pestaña o flagelo parte del blefaroblasto, atraviesa la parte anterior del parásito pasando por su parte media y sale al exterior, prolongándose en ondulaciones hasta una extensión de las tres cuartas partes del cuerpo parasitario. Este flagelo se colorea debidamente por la solución colorante de Giemsa: mejor se colorea por la violeta genciana anilinada.

Este flagelo y la extremidad posterior acintada le sirven de órganos de locomoción y con ellos producirían los movimientos vibratorios en diversos sentidos observados en las finas partículas amilaceas emulcionadas en el latex.

Ningún borde filamentoso, ninguna membrana ondulante he podido comprobar, como los que se observan en los trypanosomas, parásitos como sabéis, muy semejantes a los leptomonas. La multiplicación se efectúa por división longitudinal, encontrándose muchas veces dos parásitos acolados por sus extremidades posteriores, final de una división.

Los primeros indicios de una división en el engrosamiento del cuerpo y la aparición de otro blesfaroblasto. Antes de completarse la división, ya se ven las pestañas que parten de los sustrosomas.

El parásito mide sin su flagelo, 14 a 15 milímetros de milimetro y de 1½ a 2 milímetros de milimetro de ancho. Las formas intermediarias son pocas, siendo la piriforme sin flagelo la más común.

Cuando se trata de formas regresivas, todas toman la forma de creciente, pierden su flagelo, su blefaroblasto y su coloración se torna más dificultosa.

He tratado de practicar inyecciones hipodérmicas e intraperitoneales en animales del latex diluído en suero fisiológico con el fin de ver si era o no posible la vida de estos parásitos en los animales; pero mis esfuerzos fueron infructuosos, porque septisemias de otra índole hacían sucumbir a los animales pocos días después de las inoculaciones. Este parásito es más corto que el Davidi, descrito por Lafont en las Euforbías; este parásito es permanente en toda la planta y en todos las de la misma especie de la región infectada; este microorganismo es un parásito de otra familia de planta muy distante de las Euforbías, es de una Asclepiadacea, por estas razones me permito darle el nombre de Leptomonas, por los caracteres generales del parásito, y de Elmassiani, en memoria de mi antiguo profesor y compañero de trabajo.

PARASITOLOGÍA DE CIERTOS ANIMALES DEL PARAGUAY.

Por LUIS E. MIGONE,

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Permítaseme presentar en este certamen científico un resumen del estudio sistemático, desde el punto de vista parasitario, de la sangre y de los órganos internos de ciertos animales del Paraguay.

He examinado, de preferencia, los animales que viven en los ríos, pantanos y lugares húmedos o anegables de mi país, sean ellos aves o reptiles, sean peces o mamíferos.

Los parásitos predominantes son las hemogregarineas, los tripanosomas, los microfilarias, los myxosporídeos y un parásito bastante mal conocido aún: los linguátulas.

AVES.

Theristicus candatus (Bodd), Ibidæ, *kuru-káu* nombre guaraní. Esta ave que se alimenta y vive en los lugares bajos y húmedos, presenta bastante tripanosomas en la sangre. Este tripanosoma es bien largo, mide tres veces el diámetro longitudinal del glóbulo rojo. Sus movimientos son rápidos. El núcleo es bastante grueso, rico en cromatina; centrosoma manifiesto, neto; el protoplasma granuloso y membrana ondulante envolviendo dos veces el cuerpo.

Fijación alcohol. Coloración sistemática Giemsa.

Butorides striata (L.), Ardeidæ, *hoko-i*. Esta ave se mantiene en los lugares francamente pantanosos, presenta tambien tripanosoma en la sangre, muy parecido al anterior.

El *Tigrisoma marmoratu* (Vieill.), *hoko-hovih* o *hoko-pará* y el *Syrigma sibilatrix* (Temma), Ardeidaes, *kuaraih-mimbih*, que también viven en los lugares pantanosos, no son parasitados.

He estudiado con mucha detención la sangre de los más comunes Anatidaes: *Metopiana peposaca* (Vieill.), *yhpé-pepó-sakú; Nettium brasiliense* (gen.), *Yhpé-i* o *yhpe-kutirí;* y del *yhpé Dendrocygna viduata* (L.), pero ninguno de ellos está parasitado.

El *tuyuyú, Tántalus americanus* (L.) uno de los más grandes zancudos tiene tripanosoma en su sangre. Este tripanosoma es tal vez un poco más grueso que el anterior pero tan largo como él.

PECES.

Nuestros ríos y lagunas son muy ricos en diferentes variedades de peces. Muchos de ellos se alimentan de vegetales o restos orgánicos de todas clases sin excepción.

Los pescados sin escamas son, en general, más parasitados.

El *Preudoplatystoma coruscans* (Agass.), Siluridæ, *surubi* o *pirá pará* en guaraní, es un pescado sin escama, bastante común en las grandes aguas, tiene la sangre infectada de hemogregarinea; la piel está atacada de myxosporideos y el canal intestinal, la cavidad peritoneal, el tejido subpleural y los músculos costales son invadidos de linguátulas o quistes de linguátula.

El *taguá* o *ytauguá*, también Siluridæ, *Doras armatus* Cuv. es muy a menudo parasitado como el *surubi*.

Otro Siluridæ, tal vez el más grande de nuestros pescados, sin escamas igualmente el *Zúngaro manguras* (Val.) *mangurudyú* o *piraguasú*, es generalmente infectado de hemogregarinea de myxosporideo cutaneo y de linguátula.

De los dasyatidæ, el *Potamotrygon humboldtii* (Roullin) o *dyavevihi*, también suele infectarse de myxospolideos.

Entre los characidaes son el *Prochilodus argentens* (Agass.) kihrihmbatá y el *Hoplias malabaricus* (Bloch) los que presentan infecciones mixtas en los órganos internos, del bazo, del hígado peritóneo y branquias de myxosporideos y linguátulas.

REPTILES.

El *dyacaré hu, Caiman sclerops* (Schneid.) es el más parasitado. En él se encuentra hemogregarinea, microfilaria en la sangre y órganos internos; en la cavidad abdominal y primeras vías respiratorias abundan los quistes de linguátulas.

Todos estos parásitos pueden ser encontrados sobre un mismo animal.

De los Teiidæ, el *tedyú hovih, Ameiva ameiva* (L.) y el *tedyú guazú, Tupinambis teguixin* (L.) son también parasitados de hemogregarineas.

De los amphisbaenidae tiene hemogregarinea el sólo ejemplar examinado: *Amphisbæna alba* (L.).

Entre los Ophideos he estudiado la sangre del *sukuri, Eunecter murinus* (L.); del *nyahaniná hú, Spillotes pullatus* (L.); de los *mboi hovihs, Phylodrias schotti* y *olfersii* Licht; del *kihrihó, Lachesis neuoviedi* (Wagl.), y todos parasitados de hemogregarineas.

MAMÍFEROS.

Los mamíferos infectados de microfilarias son el *aguará guasú, Canis jubatus* (Desm.); el carpincho, *Hydrochærus capibara* (L.); *el kihdyá, Myocastor coypus* (Mol.); el *aguará popé, Procyon cancrivorus brasiliensis* (Yering.)

Vemos, que en el centro de América del Sur existen parásitos idénticos a los ya conocidos en el viejo continente y en otras naciones americanas.

Conozco los interesantes trabajos del Profesor Carini, director del Instituto Pasteur

de São Paolo, sobre los hemogregarineas del *Mus decumanus*,[1] sobre las del Phylodias (Schotti);[2] del Tupinambis teguixin y del Caimán.

Por otra parte el Profesor Laveran y Mme. y Mr. Phisalix, se han ocupado recientemente de una manera extensa del hemogregarinea de una viperinea americana, *Lachesis alternatus*.[3]

He repetido todos estos estudios en los animales de las mismas especies existentes en mi país, y, sirviéndome éstos de base, he seguido investigando en las demás especies enumeradas.

La sangre del *Zúngaro mangurus*, del *Dora armatus* y del Pseudoplatystoma presentan una hemogregarinea uniforme, con un núcleo central característico que ocupa todo el tamaño del parásito, con muy pocas granulaciones protoplásmicas y una tenue membrana periférica. Estos parásitos se encuentran alojados en los glóbulos rojos y nunca en los leucocitos. Se desarrollan en el protoplasma celular deplazando al núcleo hacia la periferia, y, a medida que el parásito crece, el glóbulo rojo se deforma y se destruye. La gregarinea se desarrolla como un vermículo hasta abandonar el glóbulo hemático.

Cuando se observa una preparación húmeda de sangre, se ven estos desplazarse en el plasma sanguíneo, con un movimiento lento vermicular. En este estado, estado extraglobular, toman muy difícilmente una buena coloración.

En el hígado y bazo de estos animales se encuentran pequeños quistes en cuyo interior se diseñan las fases de multiplicación esquisogónica.

Aparte de la forma vermicular del parásito, se encuentran formas esféricas con rica masa cromática, que, probablemente, son individuos de sexualidad distinta.

En los glóbulos rojos no se encuentra más de un parásito, no es como la sangre de las *Lachesis alternatus* (Laveran) o en la *Lachesis neuvviedi* en que en algunos glóbulos están dos o tres alojados. Como en estos peces estudiados son sus hemogregarineas muy semejantes, creo que deben ser de la misma especie.

MYXOSPORÍDEOS.

Los myxosporídeos, tan extensamente estudiados por Buschili en ciertos peces de Europa, también se encuentran en el Paraguay.

Forman tubérculos subepidérmicos en los pescados sin escamas, en toda la pared ventral. Se consideraban en mi país como quistes de vermes, pero, disecando cuidadosamente se puede extirpar un tubérculo blanquecino, de 2 o 3 milímetros de diámetro. Con una ligera presión se rompe derramándose un líquido lechoso lleno de myxosporídeos.

Cuando el pescado es con escamas, estos tubérculos se encuentran en las branquias, en el hígado, el bazo, y el tejido subpleural.

La sangre y el tejido muscular no son invadidos por ellos.

MICROFILARIAS.

En el *Caimán sclerops*, en el *Hydrochœrus capibara* en el *Canis jubatus* y en el *Myocastor coypus*, he encontrado numerosos microfilarias en la sangre, en el bazo e hígado.

Por lo general los animales atacados de microfilarias son enfermos. Muestran algunas particularidades de vida: se alejan de los pántanos, enflaquecen y es relativamente fácil su caza porque se defienden poco.

El hígado de estos animales es más oscuro que lo normal pero sin aumentar de volumen. La bolsa biliar es grande.

La sangre y frotis de los órganos internos presentan abundantes microfilarias, envueltas en su bolsa gelatinosa, nialina o completamente desnudos. El parásito es anillado y granuloso con un núcleo periférico grueso algunos de ellos.

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[1] Revista de la Sociedade Scientifica de São Paulo, vol. 5, agosto, 1910.

[2] C. C., Septiembre, 1910.

[3] Bulletin de pathologie exotique, 1913.

Como se trata de observaciones practicadas en animales salvajes y agarrados con perros o muertos a fusil, no es posible completar las muchas fases del estudio de los microfilarias y, mucho menos, determinar sus especies.

LINGUÁTULAS.

Las linguátulas muy mal conocidos hasta ahora es bastante común en los pescados que provienen de aguas muy contaminadas de materias órganicas en descomposición. En Asunción se encuentra muy a menudo en los que vienen del Río Confuso u otros riachos próximos y en los mismos pescados del Río Paraguay también se observa. No solamente se encuentra en los pescados sino también en el caimán y otros mamíferos señalados.

Cuando se abre un pescado infectado, salta a la vista en la cavidad abdominal numerosas linguátulas y questes de pequeñas linguátulas.

El peritoneo, epiplón y peritoneo parietal, albergan comúnmente estos parásitos.

Lo particular es que parece que este Arágnido penetra por el canal gastro-intestinal. He observado repetidas veces al linguátula atravesando la pared intestinal siempre con la cabeza hacia la cavidad peritoneal.

Así como hay parásitos bien desarrollados de 1 a 3 centímetros de largo, así también hay numerosos quistes, de 1 a 3 milímetros de diámetro, conteniendo un poco de líquido y un pequeño vermículo completamente formado con sus pseudoartzos y sus buenos garfios.

Por los caracteres generales del parásito me parece ser Linguátula serrata.

Como he dicho este parásito no sólo se encuentra en los peces sino que también en los mamíferos que se alimentan de peces muertos que encuentran en los bordes de los ríos o lagunas secas, como en el *Cani jubatus* y el *Procyon cancrivorus brasiliensis*.

Posiblemente los ejemplares de linguátulas encontrado por Darling y Viana tienen origen alimentario, de peces mal cocidos o mal preparados o poca propiedad en la alimentación.

Before calling for the paper of Dr. González-Rincones on "Ascanio's method of staining parasites," I wish to announce that Dr. González-Rincones presents to the Scientific Congress, through Section VIII, a reprint with the following title: Revision del estudio de nuestro tripanosomas. Caracas: Tip, Guttenberg, 1914.

MÉTODO DE ASCANIO PARA LA COLORACIÓN DE LOS PARÁSITOS DEL PALUDISMO.

Por RAFAEL GONZÁLEZ-RINCONES,

Profesor de la Facultad de Medicina de Caracas, Venezuela.

Tengo el honor de presentar algunas preparaciones de sangre, hechas en mayo de 1915 con una técnica que mi compañero, el Dr. Ascanio, de Caracas, considera propia. Consta de los tiempos siguientes:

1°. Fijación con alcohol metílico durante un minuto (o mientras se cuenta mentalmente 110).

2°. Coloración con solución de eosina en alcohol metílico al 1 por ciento, un minuto.

3°. Lavado rápido con agua corriente para determinar la coloración definitiva de la eosina.

4°. Coloración con azul de metileno acuoso al 1 por mil (mientras se cuenta un minuto o 110, mentalmente).

5°. Lavado al chorro, secando por medio de agitación al aire.

Toda la técnica dura a lo sumo cinco minutos y los hematozoarios se muestran teñidos de azul intenso, siendo muy visible el pigmento sobre este fondo de protoplasma parasitario. La cromatina no se tiñe de rojo rubí como con el "Giemsa."

Los elementos normales de la sangre periférica se coloran así:

Glóbulos rojos: de color chocolate, rojo violáceo, uniforme.

Polinucleares eosinófilos: núcleo azul pálido; granulaciones voluminosas rojas.

Polinuclares neutrófilos: núcleo azul más intenso que en los eosinófilos; pequeñas granulaciones rosadas sobre un fondo rosa pálido de protoplasma.

Mononucleares grandes: protoplasma azul intenso con núcleo apenas coloreado de azul celeste muy pálido.

Linfocitos: núcleo azul intenso homogéneo.

Aunque la coloración en general de los glóbulos blancos es bastante parecida a la que da la triacida de Erlich, se nota que los mononucleares se coloran en sentido inverso.

La modificación aconsejada por el Dr. Ascanio tiene la ventaja de su rapidez y puede reemplazar para el diagnóstico de las plasmodiosis las soluciones de Romanowsky, Giemsa, May-Grünwald, los polvos de Jenner, Leishman, etc., que comienzan ya a escasear en el mercado de los productos químicos europeos. Sea cual fuere su grado de originalidad, me ha parecido interesante y oportuna.

The CHAIRMAN. I would like to ask the Doctor if this method has been published?

Dr. GONZALEZ-RINCONES. No; it has not been published.

Dr. GUITERAS. The method is the following: Fixation in methylic alcohol during one minute, or while we count 110 mentally; second, staining with eosin solution in methylic alcohol, 1 per cent, one minute; third, rapid washing with running water to determine the final coloration of the eosin; fourth, staining with aqueous solution of methylene blue, 1 per thousand, one minute or while we count 110; fifth, washing freely in water, drying in the air by shaking the preparation. The whole technique will take not more than five minutes, and the parasites are found stained intense blue, the pigment being quite visible upon this background of the protoplasm. The normal elements of the blood are stained as follows: Red cells, chocolate color, violet red, or uniform coloration; polynuclears eosinophile, nucleus pale blue, granules large, red; polynuclears neutrophile, nucleus blue, granules small, rosy colored on a background of pale rose of the protoplasm, nucleus more intense blue than in the eosinophiles; large mononuclears, intense blue protoplasm with a nucleus very slightly stained of a light blue, very pale; lymphocytes, nucleus intense blue, homogeneous.

The CHAIRMAN. Are there any comments on this paper? If not, I am requested to announce that the paper of Dr. T. Bayma, on "Adrenalin in Amoebic Dysentery," will be read by title.

ADRENALIN IN AMEBIC DYSENTERY.

By THEODORO BAYMA,

Director of the São Paulo Bacteriological Institute (Brazil) and Chief Physician of the Medical Clinic of the Santa Casa de Misericordia Hospital.

"On the treatment of bacillary dysentery by adrenalin" is the title of an interesting article by Dr. Franz V. Göers in the Münchner Medizinishe Wochenschrift No. 14, April, 1915.

This article studies the effects of the opiates, of atropine, of aspirin, and especially of adrenalin in a series of about 300 sufferers from bacillary dysentery. The cases are from the author's hospital practice.

He concludes that, besides its innocuousness, suprarenin has a specific action on the syndrome of bacillary dysentery, especially as regards the pains, the rebellious hiccoughs and vomiting in grave cases. The medicament in solution of one to a thousand is administered per os, 10 to 20 drops in a little water, at intervals of one to two hours, and in grave cases large intestinal washings, in the dilution of 1:100,000 or 1:500,000, at the temperature of 40° C. This application is made with a stomach tube 1 meter long and not very thick (8 mm.), the patient being in the lateral decubitus or genu cubitus, injecting as much as 800 c. c. of the solution. In addition to its action on the pains and the disappearance of blood from the feces, Dr. F. Göers mentions the improvement of the general condition of the patient and the cessation of the toxic symptoms, the cure being manifest in less than 6 or 10 hours.

This is the summary of Dr. Franz Göers's work.

Inspired by this work we sought to verify the effects of adrenalin in the treatment of amebic dysentery, a disease observed amongst us for many years, as may be verified by the publications of Lutz[1] (1888, 1889 to 1898), Vital Brazil,[2] Diogo de Faria, A. Mendouça,[3] and recently by other colleagues.

We threw ourselves more resolutely into these experiments after knowing the opinion of Kirschner, who sees in infectious diseases the principal therapeutic indication for adrenalin, as well as the observations of Pourcev[4] (of Moscow), with relation to the existence in the suprarenal glands of hyperemia, hemorrhagic effusions, diminution, and even absence of the amorphous substance, more or less marked degeneration and diminution of the fatty element in cases of dysentery, diphtheria, typhoid fever, etc.

The results of the observations which we have collected have brought us to the conviction of its specificity perhaps on intestinal and hepatic amebiasis.

One advantage of the new application of adrenalin, and which is not to be despised, is simplicity of administration, as it is not repugnant to adults, and especially children, as happens with injections of emetin.

The patients treated by us are not yet many in number, there being only a few more than 10 cases; all presented the complete dysenteric syndrome, and besides this, case X presented a suppurative hepatitis of amebic origin, proved by the presence of amebæ in the pus of the abscess.

In two cases the clinical cure was accomplished within the first 6 hours and confirmed by microscopical examination of the feces and absence of blood in the feces 20 hours after the beginning of the treatment (cases VIII and IX); in another (case VII) 24 hours after the cure was complete, clinical, microscopical, and chemical proofs. In case III the same results were obtained in 2 days; in cases I and II 4

[1] Dr. Adolpho Lutz: "Report on the work of the Bacteriological Institute during the years 1897 and 1898." São Paulo Medical Review, 1898, p. 182; 1899, p. 308.

[2] Dr. Vital Brazil: "A case of dysenteric abscess of the liver." São Paulo Medical Review, 1898, p. 6.

[3] "Bulletin of the Society of Medicine of São Paulo," 1897.

[4] Pourcev: "Pathogénie des glandes surrénales et leur lésions pathologiques." Journal d'Urologie Medicale et Chirurgicale, 1912, p. 682.

days of treatment were necessary; case V required 5 days; case VI, a chronic case, with acute remittance, of eight months' standing, with 70 to 80 evacuations daily, treated previously with emetin without result, was enabled to return to work after 10 days' treatment; the patient with abscess of the liver (case X) required 25 days for the cure to be effected.

Case IV, of more than three months' duration, was the only one which presented a certain rebelliousness to the action of suprarenin; however, if it had not been for the systematic examination of the feces, the case would have been considered clinically cured after some days of medication as it presented no vegetative amebæ. We did not consider it so, however, in view of the presence of cystic forms. Without acceding to the reiterated solicitations of the patient we detained her for the prosecution of studies as to the action of the medicament per os and in intestinal washings on that resistant form of the protozoon, consequently on ameba carriers—that is to say, on the rôle which the extract of the suprarenal capsule may play in the prophylaxis of amebiasis. Having given three intestinal lavages, with a four days' interval, we no longer observed the cysts, which argues in favor of the method in chronic and rebellious forms of the disease.

With the exception of this case, in no other did we encounter the cystic forms of the protozoon, a fact encountered with some frequency in individuals submitted to treatment with emetin.

Are we dealing in this case with a strain of amebæ that are resistant to adrenalin as has already been verified in the case of the alkaloid of ipecac? And when the amebatropic or amebacidal property of the new drug does not make itself felt on the parasite, will an "intermittent treatment" following the clinical cure be necessary, as Baermann and Heinemann[1] advise in such cases that have been treated with emetin?

We prudently initiated the experiment by administering 5 drops in the morning and 5 in the afternoon of the solution of adrenalin hydrochlorid 1:1000 of Parke Davis & Co.

Gradually and cautiously we increased the dose up to 30 drops or 1 milligram of adrenalin hydrochlorid every hour or every two hours according to the severity of the case.

We verified Dr. Göers results as to the complete innocuousness of the drug; we did not observe in any one of the patients the least symptom or phenomenon of intoxication. Furthermore, O. Josué,[2] Léon Bernard,[3] and Netter had already demonstrated that poisoning accidents should not be feared when adrenalin is administered per os or in the subcutaneous cellular tissue. Not even in case IV, an old atheromatous woman, did we have any fears of augmenting the arterial lesions, as we were convinced by Josué's demonstrations that these lesions only follow intratracheal and intravenous administration of the drug.

In acute cases treated early in the disease a large dose is not necessary as is shown by cases I and II, in which only 5 drops twice a day brought about the cure. In the case of the patient of case III we administered 5 drops every three hours. In that of case V 10 drops every two hours and in that of case VII the same quantity every three hours.

Of the observed cases VIII and IX, one in a member of our family and the other in a servant in the house, we were enabled to follow pari-passu, from the first manifestations, the effects of the medicinal action of adrenalin, convincing us still more of its high therapeutic value in amebic dysentery, and even of its specific action. The cure of these two cases was accomplished within six hours by the administration of 10 drops of the solution at two-hour intervals.

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[1] Baermann-Heinemann, "Die Behandlung der Amöben-dysenterie mit Emetin"—Münchner M. Wochenschrift, 1913, p. 1132-1210, Band 21-22.

[2] O. Josué, "Remarques sur l'emploi de l'adrénalin en therapeutic." La Presse Medicale 1910, p. 164.

[3] Léon Bernard, "A propos de la posologie de l'adrénalin." La Presse Medicale 1910, p. 120.

Wishing to test the action of the drug by subcutaneous administration, of which Dr. F. Göers did not cogitate, we experimented on a patient without the least result, while improvement was manifested as soon as the gastric route was used, 20 drops being administered every two hours.

The rapid improvement experienced by patients after the first doses of the drug impresses one greatly; the general condition is improved, the colic and tenesmus are lessened immediately or even disappear, the number of evacuations is diminished. The latter in a few hours fail to recur (cases VII, VIII, and IX) and lose their mucosanguinous character, becoming pasty or even normal, without the characteristic odor of rotten leather, free from blood, amebæ and cysts of this protozoon.

Case VI deserves close attention, the chronicity of which (8 months duration) proved the high curative power of suprarenin in ascending doses (10 to 20 drops), accomplishing a cure in 10 days, while months of treatment with emetin brought about only an insignificant improvement.

Also in case IV, the intercurrence of a pleuro-pneumonia in an organism impaired by age and by a long and serious illness, causing old Isabel to succumb, provided us with one more irrefutable proof of the pharmaco-dynamic action of adrenalin in intestinal amebiasis.

The restitution of the integrity of the large intestine pictures the energy which the drug exercised, for about a half dozen small open ulcers remained, mere vestiges of the myriads which were present and which healed by a cicatrizing process, evidently very recent. The histologic examination of the large intestine, made by Dr. Dorival de Camargo, of the Butantan Institute, did not reveal the presence of amebæ or cysts in the sections.

The feces following the first administrations of the drug assume at times a dark color, as if they were highly bilious, a coloring which stains intensely the bacilli present, and which becomes progressively fainter.

In some cases (Nos. VI, VII, and VIII) we noted strong constipating action which required the use of a purgative to render the intestinal functions normal.

We should not omit one fact in regard to adrenalin, and which was already noted in regard to emetin, and which appears to be connected with the source or quality of the drug. As we know, there is synthetic adrenalin and extractive adrenalin, the latter more active than the former.

It is thus that in case IX, a case which evolved under our eyes, we first employed a Brazilian solution of adrenalin and later a solution sold as prepared by Clin of Paris, without the patient experiencing the slightest relief from the colic and tenesmus which were severe enough to bring tears to the patient's eyes. Substituting these preparations by that manufactured by Parke Davis, all symptoms gradually lessened and finally disappeared, the patient attending to her duties within a few hours.

As regards case IV, we must note in passing that he was suffering from ankylostomiasis also and that the drug had no effect on this nematode, as the ova were always found in the feces.

How can the action of adrenalin on these two kinds of dysentery—bacillary and amebic—be explained? Dr. F. Göers thinks that, in the former, this drug exercises an antitoxic action on the toxins secreted by the bacillus, as A. Marie had shown in the case of diphtheria and tetanus toxins.

This conclusion of Marie's [1] deserved the contradiction of Dr. J. M. Stutzer [2] who holds that the neutralizing action of the adrenalin hydrochlorid on the diphtheria toxin is due to the free hydrochloric acid present and when this is neutralized the toxin is rendered indifferent.

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[1] Glandes surrenales et toxi-infections, cited by "Zeitschrift für Immunitätsforschung und Experimentelle Therapie," 1913, Band XLII, p. 420.

[2] Ueber die Wirkung von Adrenalin auf Bakterien-und Diphterietoxin, "Zeitschrift für Immunitätsforschung und Experimentelle Therapie," 1914, Band XXII, p. 372.

Such an interpretation does not appear to be acceptable to us in regard to amebic dysentery, and hence we venture to formulate questions which subsequent studies may succeed in answering.

(*a*) Will adrenalin, by its vaso constrictor action, causing an ischaemia of the vascular network of the intestine, withhold from the protozoon its favorite aliment—erythrocytes—causing it to perish by inanition?

(*b*) Has it a direct parasitropic action on the vitality of such a frail and delicate organism, as Maurel [1] thinks is the case with emetin and which Edward B. Wedder (1910) and Wherry (1912) demonstrated *in vitro* in as high dilutions as 1 to 200,000?

(*c*) Are we confronted with cases in which organotherapy, stimulating or supplying the functional deficiency of the supra renal glands, organs essential to life, as Brown-Séquard showed in 1856, and balancing the organism's deficit of epinephrin, thus reestablishing its protective functions?

(*d*) Or will all of these factors act simultaneously, each within its own sphere, on the vital conditions of the parasite?

CASE REPORTS.

Case I.—Santa Casa de Misericordia Hospital, first women's ward, case card No. 4330. Lucia B., Italian, 45 years old, widow, resident in the capital. Admitted on the 25th of April, 1915. She had been ill for 8 days, having 10 to 15 evacuations in 24 hours. Complete dysenteric syndrome. The examination of the feces under the microscope revealed the presence of blood and many entamebæ histolytica of Schaudin in active motion and engulfing many erythrocytes. Temperature and urine normal. There not being any emetin in the hospital's pharmacy, we prescribed a saline purgative, and afterwards a mixture of syrup of ipecac, with ergotin and syrup of opium, a prescription which she continued to use, with slight modifications, until May 25—that is, for one month—without showing improvement. May 26, we prescribed for the first time the 1 to 1,000 solution of adrenalin, 5 drops in the morning and 5 in the evening. May 27, 28, and 29, the same medication was continued and the patient experienced rapid improvement as regards the colic and tenesmus. May 30, the feces, of normal appearance and consistency were examined and found negative for blood and amebæ and remained so until the day the patient left the hospital. Cured by adrenalin in four days.

Case II.—Santa Casa de Misericordia Hospital, first women's ward, case card No. 5409. Estherina M., Italian, married, 42 years old, resident in the capital. Admitted May 25, 1915. Had been ill for 15 days. Temperature normal. Complete dysenteric syndrome. Under the microscope the stools showed many amebæ in motion, and blood, also eggs of ascaris. May 26, we prescribed a saline purge. May 27, we began the treatment with the 1 to 1,000 solution of adrenalin, 5 drops in the morning and 5 drops in the evening and this was kept up until June 2, when amebæ cysts and blood were no longer found in the feces, which proved to be normal. Cured by adrenalin in four days.

Case III.—Santa Casa de Misericordia Hospital, first women's medical ward, case card No. 5537. Maria da L., Portuguese, married, 35 years old, resident in the suburb of Belemzinho. Admitted May 26, 1915. She had experienced the dysenteric syndrome for 8 days. Temperature and urine normal. May 29, the examination of the feces showed blood, entamebæ histolytica in motion and phagocytised erythrocytes. We prescribed 5 drops of the 1 to 1,000 adrenalin solution every 3 hours. May 31, feces normal, negative for amebæ, blood, and cysts, and remained so in the subsequent examinations. Cured by adrenalin in two days.

[1] Contribution à l'etude experimentale du chlor d'émetine. Bulletin de l'Académie de Médicine de Paris, No. 12, March, 1914.

Applications therapeutiques.

Case IV.—Santa Casa de Misericordia Hospital, first women's medical ward; case card No. 5968. Isabel A. de J., Brazilian, 70 years old, widow, resident in the capital. Admitted June 10, 1915. A saline purgative was prescribed for her. She had been ill for more than 3 months, and experienced successive poussées of the dysenteric syndrome, frequently expelling muco-sanguinous feces of very bad odor. General condition bad; great impoverishment and profound asthenia. Tongue covered with a thick greasy coating. Belly painful to touch. June 11, the examination of the feces showed them to be of a muco-sanguinous character, very foul smelling and under the microscope, ova of ankylostoma, and many other flagellates besides, a large amount of pus and blood and many amebæ histolytica of Schaudin in motion and with phagocytised erythrocytes. June 12 and 14, I prescribed 15 drops of adrenalin solution every 3 hours. The colic and tenesmus disappeared and the feces became less fetid.

June 15 we increased the number of drops to 20. The evacuations became less frequent and of a dark color and the amebæ, fewer in number, were immobile. The patient was in good spirits, manifesting a general improvement. June 22, still great quantity of pus, very little blood, and very few amebæ, and these motionless and with granular endoplasm and without phagocytised erythrocytes, which we had noted since the 15th. Three evacuations a day, less dark in color. June 27, no evacuation. The patient feels quite well and asks for solid food. The general condition has improved very much and the tongue is completely clean. Abdomen not painful to palpate. July 1, doughy feces, without amebæ or blood. July 3, a large quantity of cystic forms of amebæ histolytica appeared in the feces. The medication per os continued until July 7, when we made the first intestinal lavage, according to Dr. F. Göers's indication. The patient expelled the solution of adrenalin half an hour afterwards, along with hard feces, of a normal color and in which we found the cysts. July 12, one doughy stool per diem, still with cysts. We gave a second washing and recommended the medication per os suspended on July 7. From this date until the 16th the patient only had one evacuation. July 16 we gave a third lavage. July 17 and following days we did not observe any more cysts, amebæ, or blood in the feces, the patient evacuating naturally on alternate days. The patient feeling well and strong, insisted on being discharged, but this was not permitted, in order to keep her under observation for further study. July 20, the patient got chilled, developed a cough and a stitch in the left axillary region. Temperature, 37.8° C. July 21, auscultation revealed the phenomena of a left pleuropneumonia. Temperature, 38.4; feces negative. The patient got worse of the pleuropulmonary affection, dying on the 24th at 6 o'clock in the morning.

Autopsy: It was not possible to make a complete autopsy, so that only the large intestine, the appendix, and kidneys, with their respective suprarenal bodies, were taken out. Liver and kidneys showed no macroscopic alteration. Appendix and diverticulum normal; also the abdominal ganglia. The large intestine was opened and we removed from it some doughy feces of normal appearance, which we examined for amebæ and cysts according to Dr. K. Ujihara's method,[1] since the microscope did not reveal them to us, but without any results. The whole extension of the intestinal tract from the cæcum to the anus, especially in the lower portion, was riddled with small lenticular points, with the surface covered with a thin and slimy epithelial coat, showing that there had been a very recent process of cicatrization in these healed miliary ulcers. In one or another section a few of these small ulcers (half a dozen, perhaps) are found still open, the largest of which did not exceed in size a grain of rice, round or oval in shape, with the edges mined or cut perpendicularly

[1] Studien über die Amöbendysenterie, Zeitschrift für Hygiene und Infectionskrankeiten, 1914, Band 77, p. 329.

and the floor constituted by the muscular coat. Scraping with the knife point under the edges, no amebæ histolytica were found in the material thus obtained.

Sections of the large intestine, made by our colleague, Dr. Dorival de Camargo, assistant of the Serumtherapeutic Institute of Butantan, did not reveal the presence of the parasite, either in its vegetative form or in its cystic form.

As regards the suprarenal glands, macroscopically altered, let us await the results of the histopathological examination to say something about them in the prosecution of our studies. We shall then treat of the experiments in vitro as regards the action of adrenalin on the amebæ and of its degenerative forms observed during the treatment, subjects which do not belong to the properly clinical feature of this work.

Case V.—Santa Casa de Misericordia Hospital, first women's medical ward; case card No. 6448. Olympia da C., Portuguese, 34 years old, married, resident in the suburb of Cambucy. Admitted June 26, 1915; six months pregnant. Urine showed trace of albumen and much pus. Temperature normal. Suffering from dysenteric syndrome, sometimes more, sometimes less intensely. The feces under the microscope showed a great deal of blood and many amebæ in active motion, and phagocytised erythrocytes. June 28, began to use 10 drops of the adrenalin solution every two hours. June 29, evacuated three times without colic or tenesmus. The feces became dark in color. A few nonmotile amebæ with granular protoplasm; very little blood. July 1, two evacuations with few amebæ and small amount of blood. July 3 and 4, three evacuations, nearly normal in appearance and without amebæ or blood. July 5, at the patient's request she was discharged. July 15, examination of feces failed to show any amebæ, blood, or cysts. Cured by adrenalin in 5 days of treatment.

Case VI.—Antonio R., Italian, married, 32 years old, resident in the capital. On June 5 he came to the clinic informing us that he had been sick since October, 1914. General condition bad; very pale and thin. He presents the complete dysenteric syndrome with 70 to 80 muco-sanguinous stools daily. He could not even sleep because of the severe colic and tenesmus which torment him. He was treated for several months by another colleague, who gave him some injections of emetin, with but little benefit, and for this reason he abandoned the treatment. The feces having been examined on the same day, we found many entamebæ histolytica in motion and a large quantity of erythrocytes. We prescribed 10 drops of 1 to 1,000 adrenalin solution (Parke Davis) every three hours. June 6, he returned and said that he had evacuated 30 times, with less colic and tenesmus, so that he had succeeded in sleeping some, which he had been unable to do for a long time. The medication was continued. June 7, feces contained less blood and fewer amebæ. We increased the dose to 20 drops every three hours. June 8, had 17 evacuations almost without tenesmus. June 9, evacuated only 10 times; very few nonmotile amebæ with granular ondoplasm. Very little blood. June 15, only evacuated once. No amebæ or microscopic or occult blood, and the feces remained so during the succeeding days. July 22, we had an opportunity of examining his feces on this date and found no blood, amebæ, or cysts, the latter having been looked for by Dr. Martin Ficker according to Dr. K. Ujihara's method. Cured by adrenalin in 10 days.

Case VII.—Martiniano Z., Brazilian, single, 20 years old, resident in the city. He came to the dispensary on June 3, saying he had been sick since the 1st of the month with colic, frequent muco-sanguinous stools accompanied by severe tenesmus. The microscopic examination showed a great quantity of amebæ and blood. We prescribed for him 10 drops of adrenalin solution (1 to 1,000) every three hours. This he began to use on June 4. June 5, feces of normal appearance and consistency, without amebæ or even occult blood. The following day he was badly constipated. July 2, we examined the feces, which was negative. Cured by adrenalin in 24 hours.

Case VIII.—P. R., single, Brazilian, 28 years old, resident in the suburb of Santa Cecilia. On the night of July 4 he felt the first colicky pains and a frequent desire to go to stool. The stools were only bloody mucus and were accompanied by severe tenesmus. July 5, we found many amebæ in motion and large amounts of blood. At noon we began to give 10 drops of adrenalin every two hours. After the first dose of the drug he experienced immediate improvement, which became more and more marked. Up to 6 o'clock in the evening he had only two stools and these painless. No more passages until the 9th of July, when a saline purgative was given. We found no amebæ, cysts, or blood in the feces. Cured by adrenalin in six hours.

Case IX.—Anna M., Brazilian, single, 18 years old, resident in the suburb of Villa Buarque. On July 9, at night, she felt the first colicky pains with the expulsion of bloody stools every 10 minutes. July 10, we found large quantities of amebæ and blood. The treatment was begun by using a Brazilian solution of adrenalin, 10 drops every two hours. The patient did not improve and on the following day we substituted this preparation by one made by Clin & Co., but still without result, a failure which we attributed to the preparation being old. We were disappointed as we were accustomed to record immediate improvement. On July 12, we prescribed Parke Davis's adrenalin. After the first dose (20 drops) the patient began to improve and at the end of six hours left her bed and tried to work. The examination of the feces which, after the use of National and French preparations of adrenalin showed amebæ and blood, was now entirely negative. The constipating action of the adrenalin continued until the fifth day, when after a purge the feces examined were negative and remained so subsequently. Cured by adrenalin in 6 hours.

Case X.—Santa Casa de Misericordia Hospital (São Paulo), first women's medical ward, case card No. 9672; bed No. 21. Maria Ramos, Portuguese, married, 30 years old, resident in the capital. Admitted October 4. Had been sick for 8 months; presenting at all times, with greater or less severity, the complete dysenteric syndrome. General condition bad, patient very thin and debilitated; slimy tongue; the right lobe of the liver enlarged and painful on pressure, with a spot of maximum tenderness in one of the intercostal spaces. Slight edema of the overlying chest wall; scapulodynia on the same side. Temperature 38° C. on the day of admission to the hospital. She states that there is an exacerbation of symptoms in the evening, these being preceded by chills and toward night followed by profuse sweats. Urine is normal. Feces are muco-sanguinous and very foul smelling. Under the microscope great numbers of histolytic amebæ are seen and these show red blood cells which they have phagocytised.

Treatment: Ten drops of Parke Davis & Co.'s 1 to 1,000 adrenalin solution every two hours, and this dose was increased to 30 drops on the 14th, as the feces still contained blood and amebæ, though in smaller quantities.

The number of stools became progressively less, also the quantity of blood and number of amebæ until October 25, from which date on, the feces were of a pasty consistency and contained no amebæ, blood or cysts. The intestinal colic and tenesmus ceased after the first few doses of the drug. The general condition of the patient continued to improve; the edema of the chest wall disappeared, also the tenderness to pressure and the fever.

The day following the admision of the patient, I made an exploratory puncture of the liver at the site of maximum tenderness and withdrew a small quantity of pus, chocolate colored, and which showed the presence of motile amebæ when examined under the microscope.

On November 6 I stopped the medication, discharging the patient, who left the 13th, strong, robust, with a good color, and without having shown any more amebæ or cysts in the feces, which had returned to normal.

Cured of dysentery and of a suppurative hepatitis, of amebic origin, by adrenalin in 25 days.

CONCLUSION.

First. Beside emetin, and perhaps with advantages over it, there exists another drug of great therapeutic value in the treatment of amebic dysentery—adrenalin.

Second. Adrenalin appears to have also a therapeutic effect on suppurative hepatitis of amebic origin.

The CHAIRMAN. This brings us to the end of our scientific program. Is there any special matter to come before the section? If not, the session is adjourned.

Adjourned at 12.15 o'clock.

GENERAL SESSION OF SECTION VIII.

NEW EBBITT HOTEL,
Friday afternoon, January 7, 1916.

Chairman, H. R. CARTER.

The session was called to order at 2 o'clock by the chairman.

The CHAIRMAN. The first paper on the program is by Dr. Hoffman on "The Mortality from cancer in the Western Hemisphere."

THE MORTALITY FROM CANCER IN THE WESTERN HEMISPHERE.

By FREDERICK L. HOFFMAN,
Statistician, The Prudential Insurance Co. of America.

INTRODUCTION.

The progress of society is largely measured by the more or less effective prevention of poverty, sickness, and premature death. Within a single generation a veritable revolution has been achieved in the control of many important diseases, and some of the most destructive plagues of mankind have been successfully eliminated, or materially reduced in frequency, in the principal civilized countries of the world. Foremost, in the order of importance, are the diseases attributable to infection or contagion, and in many important countries plague, cholera, yellow fever, leprosy, smallpox, typhoid fever, and tuberculosis, as well as most of the acute infectious diseases of infancy, are now measurably and effectively under sanitary control. By way of illustration, attention may be directed to the balance of mortality for four large American cities for which the data are available in a fairly trustworthy form for the last 50 years. The cities considered are New York, Boston, Philadelphia, and New Orleans, and the data may be relied upon as fairly representative for at least the urban centers of population of the country at large.

DECLINE IN THE DEATH RATE.

In the four cities under consideration Asiatic cholera and yellow fever have been practically eliminated. Smallpox has been reduced from a former rate of 39.5 to a present rate of only 2.4 per 100,000 of population. Scarlet fever, diphtheria and croup, typhoid fever, and pulmonary tuberculosis, as well as the diseases of the stomach and intestines, have materially decreased during the last quarter-century, compared with the 25 years preceding the year 1889. The most significant exception to a general decline in the death rate is the increasing mortality from cancer. In the four cities

under consideration the cancer death rate has increased from 46.4 to 72.1 per 100,000 of population. In other words, there has been an actual increase in the rate of 25.7 per 100,000 of population, equivalent to a quarter-century increase in the rate of 55.4 per cent.

Balance of mortality for New York, Boston, Philadelphia, and New Orleans, 1864–1888, 1889–1913.

[Rates per 100,000 of population.]

	1864–1888		1889–1913	
	Deaths.	Rates.	Deaths.	Rates.
Smallpox	23,799	39.5	3,308	2.4
Asiatic cholera	4,506	7.5	10	.01
Yellow fever	8,469	14.0	321	.6
Scarlet fever	39,983	66.3	25,560	18.8
Diphtheria and croup	74,274	123.2	70,396	58.3
Typhoid and typhus fevers	32,042	53.1	33,573	24.7
Pulmonary tuberculosis	220,048	364.9	303,362	223.3
Pneumonia	113,712	188.5	315,648	232.0
Stomach and intestinal diseases	164,598	298.6	266,991	196.2
Heart diseases	62,565	103.7	223,991	164.6
Nephritis	47,479	78.7	179,258	131.7
Cancer	27,305	46.4	98,085	72.1

INCREASE IN CANCER.

In the registration area of the United States, during the decade ending with 1912, the death rate from cancer was 72.8 per 100,000 of population, or 55.7 for males and 90.6 for females. In the registration area, which now includes about two-thirds of the entire American population, the cancer death rate has increased from 62.9 per 100,000 of population during 1900 to 78.9 during 1913. On the basis of a conservative estimate the annual number of deaths from cancer in the entire United States is approximately 80,000. It is therefore not going too far to speak of cancer as a menace to civilization and as a disease of the very first order of present-day importance in medicine, surgery, and public health.

PROBLEMS OF CANCER CONTROL.

Largely upon the basis of the statistical evidence regarding cancer frequency and cancer increase throughout practically the entire civilized world, a movement was inaugurated within very recent years effectively to arouse public interest in the possibilities of cancer prevention and cancer control. Chiefly under the direction of the American Society for the Control of Cancer, but in hearty cooperation with National, State, and local medical and surgical societies, a campaign of education has been carried on through the entire country, which, in the opinion of those best qualified to judge, has been decidedly beneficial and warrants favorable anticipations regarding ultimate results. Under the auspices of the American Society for the Control of Cancer, the American Medical Association, medical societies, State and municipal boards of health, etc., and several of the large American life insurance companies, a considerable amount of well-considered and instructive information on the cancer problem in its relation to the individual has been published and made available to many who otherwise could not have been reached so effectively and in so brief a period of time. Since the appeal to the public rests largely upon the statistical facts of the cancer situation, conservatively determined by a qualified analysis of the available information, it has seemed advisable to present on this important occasion, a plea for the general acceptance of the principles and methods of the American Society for the Control of Cancer, at least throughout the countries of the western hemisphere.

Cancer Mortality — United States Registration Area

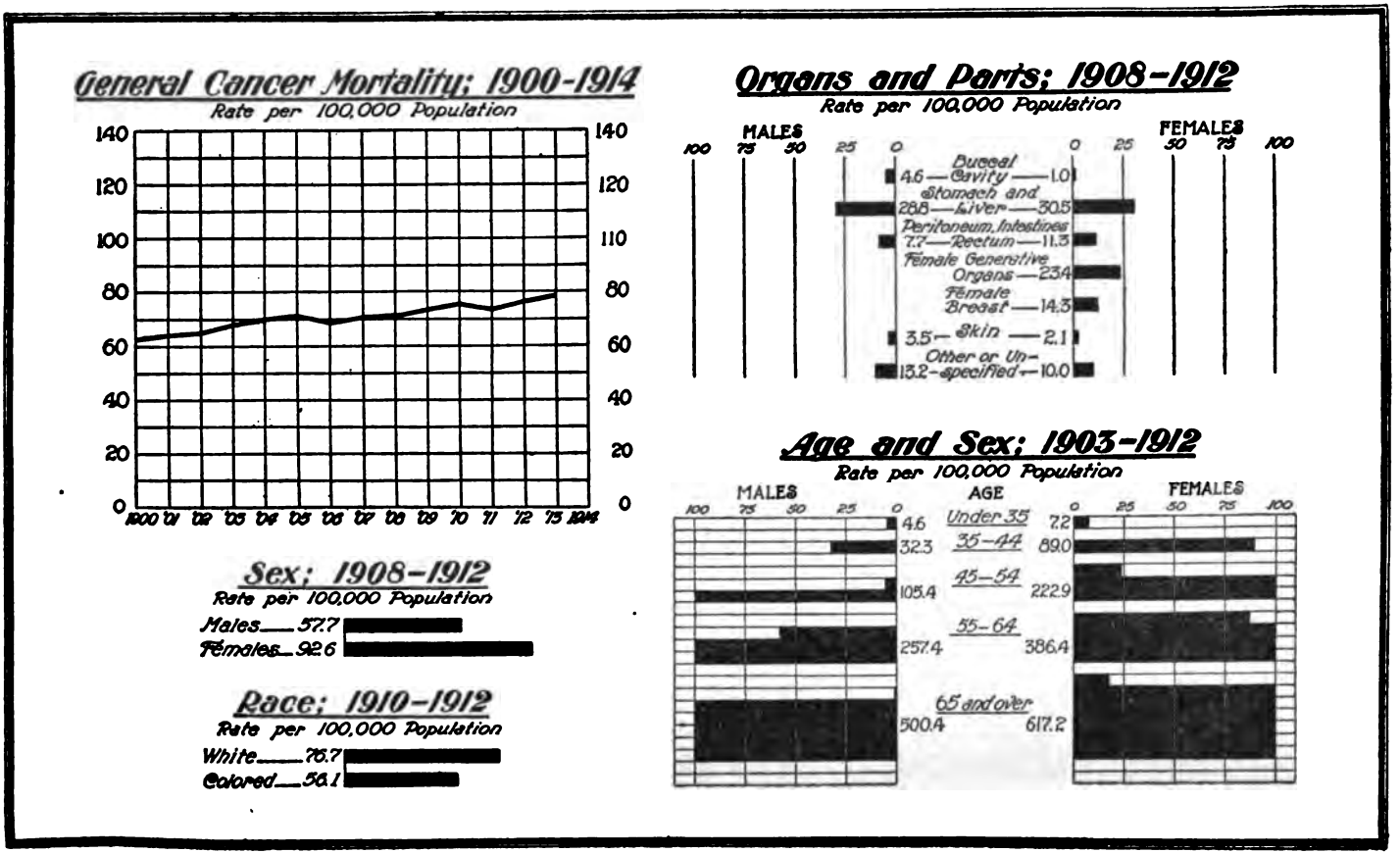


FIG. 1.

GEOGRAPHICAL INCIDENCE.

The frequency of cancer, geographically considered, varies enormously throughout the world, but the mortality rate is also decidedly affected by sex, age, race, and marital condition. Apparently less important factors are climate and occupation. For many important countries no trustworthy data are at present available and for most of the States of the Western Hemisphere the acceptable returns are limited to large cities. When all the available statistics for the civilized world are combined, it appears that during recent years (1908–1912) the average cancer death rate was 65.7 per 100,000 of population for the Western Hemisphere, which compares with a rate of 72.8 for the Eastern Hemisphere. In the Western Hemisphere the country of most importance, whether considered by area or population, is naturally the United States, but even for this country there are at present trustworthy mortality data for only two-thirds of the population, and 40 per cent of the total area. It is, therefore, not feasible to make a thoroughly satisfactory presentation of the facts of geographical incidence for the entire Western Hemisphere, but the available amount of information is sufficient for the present purpose. Preliminary, however, to a discussion of the variations in the cancer death rate throughout the Western Hemisphere, certain elementary statistical considerations, based largely upon the cancer mortality statistics of the United States registration area, are entitled to presentation.

AGE AND SEX.

The table following exhibits the mortality from cancer by age and sex in the United States registration area for the decade 1903–1912. According to this table the death rate is practically the same for both sexes at ages under 5, a trifle higher for males at ages 5 to 14, but at ages 15 to 44 the male rate is 13.6 per 100,000 of population and the female rate 32.1; or, in other words, the female rate is 18.5 per 100,000 of population, or 136 per cent, in excess of the male rate. At ages 45 and over the male rate is 236.5, against 366.4 for females; or, in other words, the cancer death rate of females at this age period is 129.9 per 100,000 of population, or 54.9 per cent, in excess of the male rate. This excess in the adult cancer death rate of women is largely, in the United States at least, due to cancer frequency in organs or parts peculiar to the female sex. The table on the following page exhibits the cancer mortality by organs and parts, in the United States registration area, for the period 1903–1912, with an estimate of the number of deaths from cancer for the different organs and parts, according to sex, for the year 1915.

Mortality from cancer, by age and sex, United States registration area, 1903–1912,

[Rates per 100,000 of population.]

Ages.	Rates.	
	Males.	Females.
Under 5	3.3	3.0
5 to 14	1.7	1.3
15 to 44	13.6	32.1
45 and over	236.5	366.4

ORGANS AND PARTS.

According to this table the rate of mortality from cancer of the stomach and liver is almost the same for both sexes, but there is a decided excess in the case of females in the mortality rate from cancer of the peritoneum, intestines, and rectum. The rate of mortality from cancer of the skin and of the buccal cavity is higher among men

than among women, but the actual number of deaths from this group of malignant diseases is not of so much importance. The excess in the female cancer mortality is to be found chiefly in the deaths from cancer of the generative organs and of the female breast, accounting for 39.3 per cent of the total mortality from cancer among women, and 35.6 per 100,000 of population of females separately considered. Eliminating cancer of the generative organs and of the breast, it is shown that the cancer death rate for males was 55.7 per 100,000 of population, against 55.0 for females; or, in other words, the actual differences in the rates were relatively of small significance.

As will subsequently be shown, these differences in the incidence of cancer by sex vary widely throughout the world, and it is in the direction of geographical pathology that the outlook is most encouraging that future statistical research will add materially to our understanding of the conditions and circumstances accountable for a high or low cancer death rate.

Mortality from cancer, by organs or parts, United States registration area, 1903–1912, and estimated cancer mortality of the Continental United States, 1915.

[Rates per 100,000 of population.]

	Number of deaths 1903–1912.	Per cent.	Rates.	Estimated number of deaths 1915.[1]	Per cent.
Males:					
Buccal cavity	9,652	7.4	4.2	2,608	8.1
Stomach and liver	64,049	49.4	27.5	15,622	48.6
Peritoneum, intestines, and rectum	16,615	12.8	7.1	4,503	14.0
Skin	7,722	5.9	3.3	1,808	5.6
Other or not specified organs	31,746	24.5	13.6	7,577	23.6
Ages 45 and over	111,884	86.2	236.5	28,135	87.6
Total all ages	129,784	100.0	55.7	32,118	100.0
Females:					
Buccal cavity	2,163	1.1	1.0	541	1.1
Stomach and liver	64,685	31.9	29.0	16,050	33.5
Peritoneum, intestines and rectum,	23,137	11.4	10.3	6,110	12.8
Generative organs	49,747	24.6	22.3	12,348	25.8
Breast	29,685	14.7	13.3	7,235	15.1
Skin	4,306	2.1	1.9	958	2.0
Other or not specified organs	28,698	14.2	12.8	4,640	9.7
Ages 45 and over	164,673	81.4	366.4	39,456	82.4
Total all ages	202,421	100.0	90.6	47,882	100.0

[1] Estimated on the basis of the percentage distribution of the mortality from cancer in the registration area in 1913.

URBAN AND RURAL.

In the registration States of the United States during the decade ending with 1912 the urban mortality rate from cancer was 79.2, against a rural rate of 66.7, per 100,000 population. The urban rate is partly affected by cancer deaths in hospitals and special institutions for cancer treatment, but when due allowance is made for this factor there would seem to be no reason to question the conclusion that cancer is relatively more common among American city population when compared with the corresponding population of the country. Important exceptions, however, are met with in different countries of the world, and the present conclusion applies only to the registration States of the United States registration area. Crude death rates in this respect are quite likely to be misleading in that the proportion of aged persons is almost everywhere larger in the country districts than in the cities.

RACE.

During the period 1906–1912, in 30 large southern cities of the United States the cancer mortality rate of the white population was 80.3 per 100,000 of population, and of the colored population, 55.2. All the available statistics for the United States and

other countries emphatically sustain the conclusion that cancer, generally considered, is relatively rare among primitive races. In the case of the American negro, for more than a century and a half in close contact with the white race, and with habits of life closely conforming to those of the Caucasians, there has been a gradual approach in the cancer death rate toward the rate common to the white population, and for cancer of the uterus the rate for the negro population of at least certain American cities is now in excess of the corresponding rate for white women. The lesser liability to cancer among primitive races would, therefore, seem to be rather attributable to habits of life or the mode of living than to racial immunity. Of all the statistical elements of the cancer problem the racial aspect of the disease is extremely interesting and most likely to prove of the first order of practical importance. Several careful investigations have been made in the United States with reference to the occurrence or relative frequency of malignant diseases among North American Indians and the Eskimos of Alaska and Labrador, but without exception the results have been negative. In other words, there are no reasons for questioning the statement that cancer is actually as well as apparently very rare among North American Indians and Eskimos, and that the explanation for the infrequency of the disease is, most likely, that it is due to habits or mode of life rather than to racial immunity.

The possible correlation of latitude and equivalent climatic conditions to cancer frequency is shown in the table following, illustrating the mortality from cancer in 130 cities, according to latitude, for the Eastern and Western Hemispheres, for the period of 1908–1912:

Mortality from cancer in cities, according to latitude, Eastern and Western Hemispheres, 1908–1912.

Degree of latitude.	Eastern Hemisphere.			Western Hemisphere.		
	Number of cities.	Rates per 100,000 population.	Index number.	Number of cities.	Rates per 100,000 population.	Index number.
60 N.–50 N.	35	105.7	98	.....	.....	.....
50 N.–40 N.	22	108.4	100	26	77.3	100
40 N.–30 N.	6	66.9	62	18	85.5	111
30 N.–10 N.	3	13.6	13	4	77.2	100
10 N.–10 S.	1	11.6	11	3	82.7	107
10 S.–30 S.	1	34.4	32	6	38.2	49
30 S.–40 S.	1	90.1	83	4	89.8	116
Total	69	98.3	.....	61	78.0	.....

According to this table there is no precise degree of correlation, partly, no doubt, because of the fact that the data for tropical countries are too insufficient, and that such cities as Calcutta, Hongkong, and Singapore are not strictly comparable with cities like New Orleans, Habana, and Paramaribo. Furthermore, 60° to 50° north latitude in European countries corresponds rather to 50° to 40° north latitude in the Western Hemisphere, as regards climatological conditions. It has not been feasible for the present purpose to establish, on the basis of a sufficient amount of statistical information, the precise correlation of temperature, rainfall, and humidity to cancer frequency, but the suggestion may be made here that such a study would add a useful contribution to cancer knowledge.

HABITS AND ECONOMIC CONDITIONS.

The question may also be raised as to whether the observed differences in the relative frequency of cancer between civilized and primitive man are not primarily conditioned by habits of life, chiefly, of course, diet, which is largely a matter of material well-being. Native races are generally underfed, at least with regard to

what in civilized countries is normally considered a nutritious diet, often, however, erroneously confused with an excess in food consumption. At least in the case of the native American Indians it is a safe assumption that the large majority are underfed, which, however, is not necessarily equivalent to the conclusion that they are undernourished, for, broadly speaking, that is seldom the case. Such investigations as have been made to determine whether the poor, as a class, are as liable to cancer or more so than the well to do, as has abundantly been shown to be the case with tuberculosis, have all been in the negative. In other words, the available evidence is rather to the effect that cancer is chiefly a disease of the well to do and by inference a disease of civilization, which broadly speaking is measured by the attained degree of material well-being or widely diffused material prosperity. Exact statistics are unfortunately obtainable with difficulty, but a most important contribution to our knowledge has recently been made by the public health department of the city of Edinburgh, which has published the statistics of cancer and tuberculosis according to the rental of the houses occupied by the deceased. It is shown by this inquiry that of the mortality from phthisis 36.4 per cent of the deaths occurred in houses renting at less than about $50 per annum, 34.6 per cent occurred in houses renting at from $50 to $100, and 17.9 per cent occurred in houses renting at over $100 per annum. The remainder occurred in lodging houses, or the information was not given. In contrast of the mortality from cancer only 21.8 per cent occurred in the houses with the lowest rental, 37 per cent in the houses with a moderate rental, and 35.9 per cent in the houses with a rental rather indicative of the prosperous and the well to do. Furthermore, while 6.9 per cent of the deaths from phthisis occurred in lodging houses, typical of the very poor, only 0.9 per cent of the deaths from cancer occurred in this class of residences. The proportion of deaths with residences not stated was practically the same for both diseases. Restating these rather important conclusions, it would appear that the frequency of cancer deaths was about one-third less in the houses of the poor but nearly double in the houses of the well to do than in the case of those who died from phthisis, which is generally considered a disease of poverty. These observations suggest the great practical value of a further statistical study of the relation of material well-being to cancer and tuberculosis.

MARITAL CONDITION.

Among other important statistical factors which require more extended consideration in the study of the cancer problem is marital condition. A recent investigation by the registrar general of England and Wales, extending over a period of three years, seems to warrant the important conclusion that cancer of the breast and ovaries is decidedly more common among single than among married women, when proper correction is made for variations in the age distribution. In contrast, cancer of the uterus, however, is decidedly more common among the married than among the unmarried, but there are reasons for believing that if a further analysis could be made of the precise site of the disease it would be shown that the excess in the mortality of the married is chiefly limited to cancer of the cervix.

CANCER INCREASE IN OLD AGE.

Of all the factors, however, which influence the cancer death rate age is of the first order of importance. Cancer is essentially a disease of adult life, and of the 80,000 estimated deaths from cancer in the United States at all ages for the year 1915, approximately 67,600, or 84.5 per cent, occur at ages 45 and over. Since the age distribution of the population varies materially, not only for different countries, States, and cities, but also for different periods of time, it is imperative that as far as practicable, the age factor should always be taken into account. Unfortunately a recalculation of crude cancer death rates, in conformity to a standard basis of age distribution, is frequently quite difficult and often practically impossible.

The most useful statistics for the purpose of illustrating the influence of age on the cancer death rate and the changes in the rate are those for England and Wales, which for the present purpose, however, are limited to the male population and the two years 1901 and 1913. The data are set forth in the table below:

Mortality from cancer in England and Wales according to age, 1901 compared with 1903.[1]

[Rates per 100,000 of population.]

Age.	1901			1913			Index number.
	Population.	Deaths.	Rates.	Population.	Deaths.	Rates.	
Under 5	1,955,361	66	3.6	1,952,363	74	3.8	106
5 to 14	3,409,963	69	2.0	3,631,918	63	1.7	85
15 to 24	3,080,166	102	3.3	3,173,023	124	3.9	118
25 to 34	2,485,951	236	9.5	2,900,795	365	12.6	133
35 to 44	1,931,944	804	41.6	2,417,420	1,064	44.8	108
45 to 54	1,396,210	2,040	146.1	1,753,957	3,021	172.2	118
55 to 64	907,945	3,353	369.3	1,120,598	5,175	461.8	125
65 to 74	477,868	2,958	619.0	627,744	4,934	786.0	127
75 to 84	165,233	1,150	696.0	187,596	1,874	999.0	144
85 and over	17,971	113	628.8	23,090	204	861.1	137
All ages	15,728,615	10,891	69.2	17,789,004	16,918	95.1	137

[1] Males only.

According to this table the cancer death rate for males at all ages increased 37 per cent, but the most significant increases in the rate occurred at ages 55 and over, having been, respectively, 25 per cent at ages 55–64, 27 per cent at ages 65–74, 44 per cent at ages 75–84, and 37 per cent at ages 85 and over. The table warrants the conclusion, which is fully sustained by an analysis of corresponding statistics for the United States and other countries, that the increase in the cancer death rate has occurred largely in the period of advanced adult life. An extended statistical study of the details by single years reveals the fact that the increase has been far from uniform at every period of life, but that there have been many important fluctuations and variations suggestive of a real increase rather than an apparent improvement in the rate in consequence of increased accuracy in diagnosis and death certification. To illustrate this point of view more precisely a table is included, giving the rates by divisonal periods of life for the male population by single years for the entire period 1901–1913. This table is self-explanatory and requires no extended discussion.

Mortality from cancer in England and Wales according to age, 1901–1913.[1]

[Rates per 100,000 of population.]

	Under 35.	35–44.	45–54.	55–64.	65–74.	75 and over.	All ages.
1901	4.4	41.6	146.1	369.3	619.0	689.4	69.1
1902	4.4	39.0	146.8	359.6	635.7	707.6	69.6
1903	4.7	42.5	157.5	380.8	626.8	741.9	73.3
1904	4.7	40.1	153.1	382.6	645.6	771.2	74.3
1905	5.1	39.5	150.4	383.4	664.0	801.8	75.9
1906	5.1	43.4	158.8	410.1	675.7	908.5	79.8
1907	5.2	42.4	151.9	398.4	664.8	805.1	78.6
1908	5.2	41.8	161.6	401.8	700.0	845.2	82.0
1909	4.9	40.8	157.9	411.4	722.4	846.8	83.2
1910	5.4	43.6	166.9	410.1	731.0	857.8	85.7
1911	5.4	41.9	171.2	426.4	763.5	897.8	89.1
1912	4.8	43.8	168.5	448.8	775.1	939.0	91.6
1913	5.4	44.8	172.2	461.8	786.0	963.5	94.7

[1] Males only.

MORTALITY OF THE WESTERN HEMISPHERE.

The present state of international vital statistics is far from being satisfactory and conclusive. Every international comparison is more or less liable to serious errors, but particularly so in the case of the countries of practically the entire Western Hemisphere. An extended discussion of the local cancer death rate by countries, States, and cities throughout this vast area would obviously be impracticable on the present occasion, but the following observations are presented as a tentative contribution toward a more scientific and extended study of the geographical distribution of cancer throughout the Western Hemisphere. Combining the available statistics from official sources for the period 1908–1912, the average cancer frequency rates for the principal geographical divisions were as follows:

Latitude 50° N.–40° N. includes the principal cities or States of British North America and the northern tier of the registration area of the United States, with a population of approximately 14,400,000. The average cancer death rate for this area was 77.3 per 100,000 of population.

Latitude 40° N.–30° N. includes the larger portion of the central and southern tiers of the United States registration area, with a population of approximately 6,000,000. The average cancer death rate for this area was 85.5 per 100,000 of population.

Latitude 30° N.–10° N. includes the cities of New Orleans, Habana (Cuba), Mexico City, and Caracas (Venezuela), with a population of approximately 1,275,000. The average cancer death rate for this area was 77.2 per 100,000 of population.

Latitude 10° N.–10° S., entirely within the Tropics, includes the cities of Paramaribo (Dutch Guiana), Bogota (United States of Colombia), and Guayaquil (Ecuador), with a population of approximately 240,000. The average cancer death rate for this area was 82.7 per 100,000 of population.

Latitude 10° S.–30° S. includes the principal cities of Brazil, and Santiago del Estero (Argentina), with a population of approximately 1,600,000. The average cancer death rate for this area was 38.2 per 100,000 of population.

Latitude 30° S.–40° S. includes the city of Pelotas (Brazil), the two principal cities of the Argentine Republic, and the city of Montevideo (Uruguay), with a population of approximately 2,000,000. The average cancer death rate for this area was 89.8 per 100,000 of population.

COMPARATIVE RATE OF FREQUENCY.

The general conclusion would seem to be justified that there is a decreasing rate of cancer frequency with diminishing distance from the Equator. How far this result is attributable to race and primitive conditions of life, rather than to climatological effects, can not be stated at the present time. In a general way, however, it would seem safe to assume that the effect of race is decidedly more pronounced than the result of more obscure climatological conditions such as temperature, rainfall, and humidity. No conclusive investigation has as yet been made to determine the possible correlation of latitude to cancer frequency, but the general evidence available would seem to suggest that latitude is not a pronounced factor in determining the cancer death rate. The following five tables exhibit the cancer death rate for the period 1908–1912, for typical cities of North, Central, and South America.

The first table is for the northern portion of North America and includes nine cities, with an aggregate population estimated for 1912 at 11,507,768, and a range in the cancer death rate from 50.6 per 100,000 of population for the city of Winnipeg, to 105.7 for the city of Boston.

I. Mortality from cancer in cities of northern North America, latitude 50° N.–40° N., 1908–1912.

[Rates per 100,000 of population.]

	Latitude.	Population (1912).	Rates.
	° ′		
Winnipeg	49 56 N.	159,256	50.6
Seattle	47 36 N.	268,500	55.8
Montreal	45 30 N.	484,400	65.4
Toronto	43 40 N.	414,000	72.2
Boston	42 22 N.	715,711	105.7
Chicago	41 53 N.	2,282,623	78.9
New York	40 43 N.	5,032,821	77.1
Pittsburgh	40 26 N.	550,385	66.4
Philadelphia	40 00 N.	1,600,072	85.3
Total		11,507,768	78.4

The second table is for the southern portion of North America and includes 10 cities, with an aggregate population estimated for 1912 at 3,179,647, and a range in the cancer death rate from 50.8 per 100,000 of population for the city of Memphis, to 109.7 for the city of San Francisco. In the case of the more southern American cities the race factor is of considerable determining importance.

II. Mortality from cancer in cities of southern North America, latitude 40° N.–30° N., 1908–1912.

[Rates per 100,000 of population.]

	Latitude.	Population (1912).	Rates.
	° ′		
Denver	39 41 N.	229,287	83.1
Baltimore	39 17 N.	568,391	89.5
Kansas City	39 08 N.	265,306	79.0
St. Louis	38 38 N.	709,387	81.9
San Francisco	37 48 N.	431,738	109.7
Memphis[1]	35 08 N.	136,861	50.8
Los Angeles	34 05 N.	362,541	100.9
Charleston[1]	32 46 N.	59,437	58.8
Savannah[1]	32 05 N.	67,228	55.9
New Orleans[1]	30 00 N.	349,171	84.9
Total		3,179,647	87.0

[1] In 1910 the negro population of Memphis was 40 per cent of the total; of Charleston, 52.8; of Savannah, 51.1, and of New Orleans, 26.3.

The third table includes the West Indies, Mexico, and Central America, with an aggregate population estimated for 1912 at 1,305,566. To increase the practical value of this table the same has not been limited entirely to cities, but includes a few islands, since in the West Indian island communities the urban and rural populations are considerably merged on account of the fact that the larger cities have, as a rule, the only available facilities for institutional treatment. The range in the cancer death rate of this group is from a minimum of 20.7 per 100.000 of population for the island of Grenada, and 20.9 for the island of St. Lucia, to 102.7 for the city of Habana.

III. Mortality from cancer in the West Indies, Mexico, and Central America, latitude 32° N.–10° N., 1908–1912.

[Rates per 100,000 of population.]

	Latitude.	Population (1912).	Rates.
	° ′		
Bermuda	32 00 N.	19,392	54.1
Habana	23 09 N.	353,509	102.7
Mexico City	19 26 N.	491,500	49.5
Danish West Indies	18 20 N.	26,742	91.0
St. Lucia	14 01 N.	49,205	20.9
Windward and Leeward Islands	14 00 N.	237,041	27 0
San Salvador	13 44 N.	60,000	58.0
Grenada	12 02 N.	68,177	20.7
Total		1,305,566	56.8

The fourth table is for the northern portion of South America, the six cities represented having a combined population for the year 1912 of 698,183. The range in the cancer death rate is from a minimum of 21.8 for La Paz to a maximum of 104.8 for Caracas.

IV. Mortality from cancer in cities of northern South America, latitude 10° N.–20° S., 1908–1912.

[Rates per 100,000 of population.]

	Latitude.	Population (1912).	Rates.
	° ′		
Caracas	10 31 N.	75,000	104.8
Paramaribo	5 39 N.	35,000	95 6
Bogota	4 35 N.	121,257	89.7
Guayaquil	2 11 S.	80,000	59.6
Bahia	13 00 S.	300,000	23.3
La Paz	16 30 S.	86,926	21.8
Total		698,183	52.7

The fifth table is for the cities of the southern portion of South America, the seven cities represented having an aggregate population for the year 1912 of 3,257,569. The range in the cancer death rate is from a minimum of 36.5 per 100,000 of population for Bello Horizonte to a maximum of 116.9 for the city of Montevideo.

V. Mortality from cancer in cities of southern South America, latitude 20° S.–40° S., 1908–1912.

[Rates per 100,000 of population.]

	Latitude.	Population (1912).	Rates.
	° ′		
Bello Horizonte	20 00 S.	39,845	36.5
Rio de Janeiro	22 54 S.	710,600	42.5
Sao Paulo	23 38 S.	400,000	45.4
Santiago del Estero	27 48 S.	20,580	37.5
Buenos Aires	34 36 S.	1,383,663	85.5
Montevideo	34 54 S.	355,017	116.9
Santiago de Chile [1]	35 00 S.	347,864	71.1
Total		3,257,569	72.5

[1] Population for 1909; rate for period 1905–1909.

The foregoing rates are largely in the nature of an approximation to the exact truth. It, however, may safely be asserted that the margin of error is not of sufficiently serious importance to invalidate general conclusions based upon the data presented, which, without exception, are derived from official sources. It is practically a foregone conclusion, however, that in the case of communities or cities with very low cancer death rates the chances of error in death certification and completeness of registration are more serious than in the case of communities or cities with high cancer death rates, but the range in the rates is so considerable that there can be no question of doubt but that underlying local causes account for the differences, which are too pronounced to be due in any material degree to errors in clinical diagnosis, death certification, and completeness of registration.

These data are illustrated graphically in figure 2.

VARIATIONS BY ORGANS AND PARTS.

It is realized that this statement requires some amplification, and in support thereof the following observations on the comparative rate of cancer frequency, with a due regard to sex and organs or parts affected, for a few selected cities of North, Central, and South America, are presented:

Mortality from cancer in cities of North, Central, and South America, by organs and parts, according to sex.

[Rates per 100,000 of population.]

Organ or part.	North America.			Central and South America.			
	New York.	New Orleans.[1]	San Francisco.	City of Mexico.	Rio de Janeiro.	Montevideo.	Buenos Aires.
Males:							
Buccal cavity	4.7	7.8	10.6	2.7	3.9	5.5	6.5
Stomach and liver	30.9	27.5	54.1	7.3	10.0	77.9	53.5
Peritoneum, intestines, and rectum	10.3	6.4	13.7	2.4	1.7	7.3	4.5
Skin	1.8	1.5	2.5	1.8	2.0	1.3	2.0
Other or not specified organs	15.1	32.1	20.9	13.1	13.6	35.0	31.5
All organs and parts	62.8	75.3	101.8	27.3	31.3	127.0	98.0
Females:							
Buccal cavity	.9	2.2	1.1	1.3	1.2	1.2	1.1
Stomach and liver	30.5	23.2	40.1	9.4	4.1	47.3	23.4
Peritoneum, intestines, and rectum	12.1	6.8	17.6	4.0	1.8	8.7	4.5
Generative organs	23.4	35.6	32.6	36.3	15.4	23.3	18.4
Breast	13.7	12.0	20.2	3.5	3.6	7.2	4.8
Skin	1.1	.6	2.1	.8	.9	1.2	.8
Other or not specified organs	9.8	16.9	10.6	13.3	18.8	21.1	18.2
All organs and parts	91.5	97.3	124.3	68.6	45.7	110.0	71.2

[1] The data for New Orleans are for the white population only.

The table provides sufficient material for the purpose of illustrating the very wide degree of variation in the local incidence of cancer according to organs or parts of the body affected. It can not well be questioned, for illustration, that the status of medical practice in Buenos Aires is not so very much different from the attained degree of medical and surgical proficiency in the city of New York. The table shows that the general cancer death rate of males in the city of New York was 62.8 per 100,000 of population, against 98.1 in the city of Buenos Aires. It could not well be maintained that the physicians of Buenos Aires diagnose malignant disease with much greater accuracy than the physicians of the city of New York, yet cancer among men is shown to be approximately 50 per cent more frequent in Buenos Aires than in New York City, and upon further analysis it appears that most of this excess is due to the higher degree or rate of frequency occurrence in the case of cancer of the buccal cavity, stomach and liver, skin, and ill-defined or nonspecified organs

or parts. The disease, however, is less frequent in Buenos Aires than in New York City in the case of cancer of the peritoneum and intestines and rectum. For this group of cancers the death rate for the city of New York is more than twice the male corresponding rate for the city of Buenos Aires.

In marked contrast the female cancer death rate of the city of New York is 91.[illegible] per 100,000 of population, against a corresponding rate of 71.2 for the city of Buenos Aires. Considered in detail, it appears that the only form of cancer more common among the women of Buenos Aires is cancer of the buccal cavity, but the excess is very slight. The excess in the rate for ill-defined or not specified forms of cancer can not be relied upon as entirely conclusive. In a general way, all important specified forms of cancer are less common among the women of Buenos Aires than among the women of New York City, and particularly so is the case in cancer of the peritoneum, intestines and rectum, and the female breast. The analysis would seem to prove that the differences in the rates are due to local conditions, chiefly, no doubt, variations in habits of life and the possible effect of race and climate, rather than to pronounced or numerically important errors of clinical diagnosis and death certification.

These data are illustrated in Figure 4.

CANCER IN THE UNITED STATES AND URUGUAY.

As a further contribution to this very interesting aspect of the geographical study of cancer frequency, and as evidence of the great practical value of an extended statistical analysis of the official returns, the following comparative table is included for the United States registration area and for Uruguay:

Mortality from cancer in the United States registration area and the Republic of Uruguay, by organs and parts, 1906–1910.

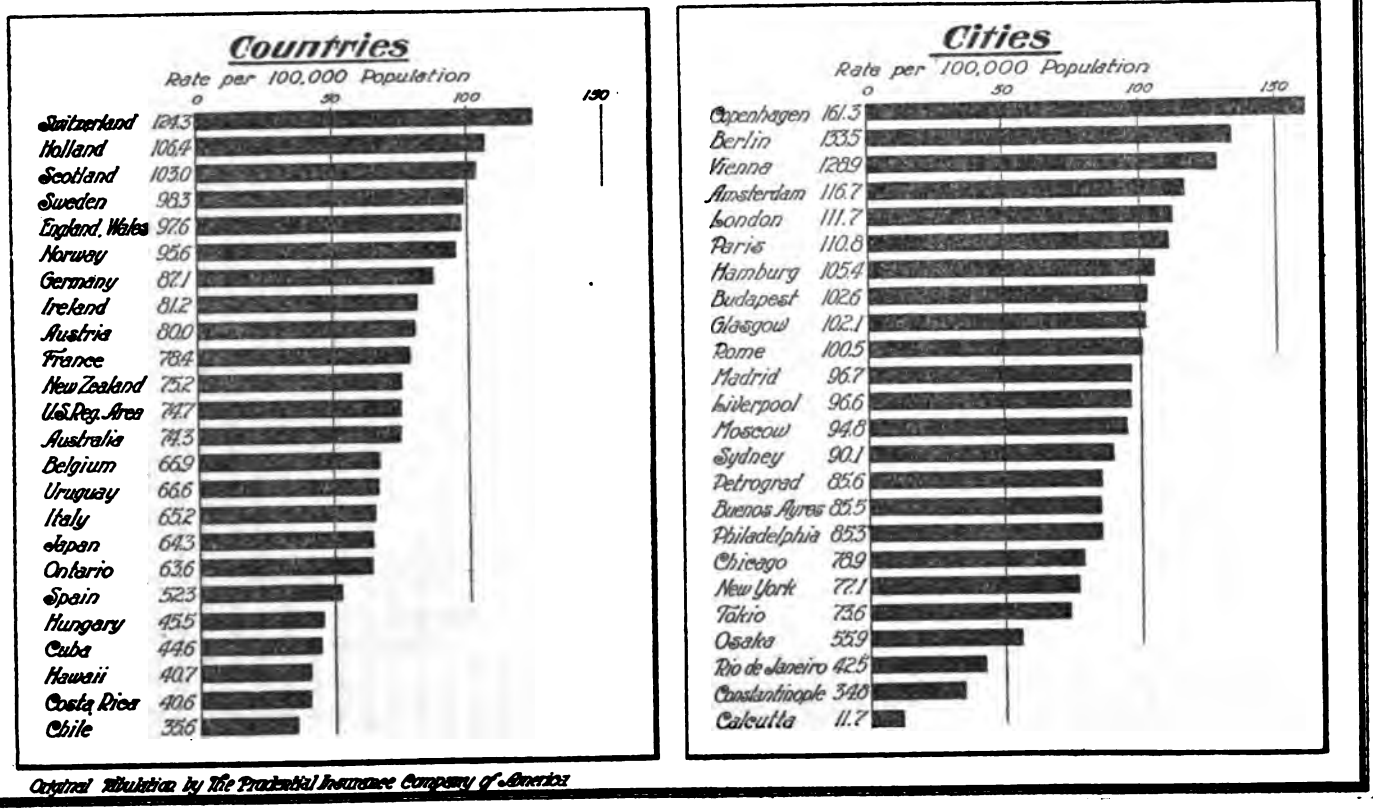
[Rates per 100,000 of population.]

	Males.		Females.		Males and females.	
	United States.	Uruguay.	United States.	Uruguay.	United States.	Uruguay.
Buccal cavity	4.2	3.6	0.9	0.4	2.6	2.0
Stomach and liver	27.6	44.4	29.0	26.5	28.3	35.6
Peritoneum, intestines, and rectum	7.1	4.2	10.5	4.9	8.8	4.6
Female generative organs	.....	.....	22.1	12.2	10.8	6.0
Female breast	.....	.....	13.3	3.7	6.5	1.9
Skin	3.4	1.6	1.9	.5	2.7	1.1
Other or not specified organs	13.4	19.4	12.4	10.2	12.9	14.9
All organs and parts	55.7	73.2	90.1	56.4	72.6	66.0

The general cancer death rates of the two countries are not very far from being about the same. The rate for Uruguay was 66 per 100,000 of total population during the period under consideration, against a rate of 72.6 for the United States registration area. Considered, however, by four groups of specified organs or parts, it appears the the rate for cancer of the stomach and liver was 28.3 per 100,000 of total population for the United States registration area, against 35.6 for Uruguay. It could not well be maintained, without the risk of successful contradiction, that cancer of the stomach and liver is less accurately diagnosed in the United States than in the South American Republic. The mortality from cancer of the skin was 2.7 per 100,000 of total population in the United States registration area, against a rate of 1.1 for Uruguay. Since this form of cancer is the most easily diagnosed, it is reasonable to suppose that the differences in the rate can not be attributed to the serious shortcomings of medical practice in the South American Republic.

These data are illustrated in Figures 1 and 3.

International Statistics of Cancer Mortality, 1908–1912



Original tabulation by The Prudential Insurance Company of America.

FIG. 2.

FEMALE GENERATIVE ORGANS AND BREAST.

The mortality from cancer of the female generative organs was 22.1 per 100,000 of female population for the United States registration area, against a rate of 12.2 for Uruguay; and the corresponding rates for cancer of the female breast were 13.3 for the United States registration area, against only 3.7 for Uruguay. No evidence is available to prove that cancer of the female generative organs is less accurately diagnosed in Uruguay than in the United States, if the higher rate for cancer of the stomach and liver in Uruguay can be relied upon as evidence that the diagnosis of a somewhat similar group of generally inaccessible cancers is as accurately made as in the United States.

The very low mortality from cancer of the female breast in Uruguay can not be accepted as proof of inaccuracy or incompleteness of diagnosis, since this is one of the most easily diagnosed forms of malignant disease. By way of further illustration, it may be stated in this connection that the mortality from cancer of the female breast is 4.5 per 100,000 of female population for the island of Cuba, but only 1.8 for Japan. In contrast, the rate attains to extremely high proportions in England and Wales, where it is 17.9; and in Scotland, where it is 15.4. Since the corresponding rate for the United States registration area is only 13.3, it would follow that if the low rate for Uruguay is to be considered evidence of inaccuracy or incompleteness of diagnosis, then the same conclusion applies to the United States and Japan, and a number of other countries for which, as far as known, the registration returns are as trustworthy as for England and Wales, Scotland, Switzerland, and the Australian Commonwealth. In fact, it may be said further in this connection, that the mortality from cancer of the breast for Bavaria, where the general accuracy of diagnosis can not be questioned, was only 9.1 per 100,000 of female population, and for Holland only 9.6, against, as said before, corresponding rates of 17.9 for England and Wales, and 15.4 for Scotland.

These data are illustrated in Figure 4.

ACCURACY OF DIAGNOSIS.

The foregoing observations are called for in defense of the practical use of the general cancer mortality statistics of the Western Hemisphere as an approximate indication of the geographical distribution of the disease throughout this vast area, and the modification of local cancer death rates by population, climatological conditions, habits of life, etc., as the case may be. Those who are responsible for the charge that methods of death certification are grossly defective, and that in a large number of cases the clinical diagnosis is inaccurate or seriously at fault, rely upon fragmentary data and not upon the required statistical evidence in conformity to the first and fundamental law of all statistical inquiries, and that is the law of large numbers. Most of the contributions to the medical literature on accuracy in death certification bear intrinsic evidence of superficial consideration and indifference to accepted principles of statistical inquiry. It is as wrongful a procedure on the part of a physician not trained in statistical methods to bring forward statistical arguments and far-reaching assertions based upon mere figures or data not conforming to the requirements of statistical science, as for a statistician superficially informed concerning medical matters to pass judgment on involved proplems of pathology or therapeutics. It is unquestionably of the first order of importance that the clinical diagnosis and methods of death certification should be further improved, and no one with any knowledge of the facts but will admit that present methods throughout the world are far from perfect or ideal; but the strongest possible objections lie against the increasing practice on the part of superficial and ill-informed medical writers, to indict on the one hand the entire practice of medicine and surgery as being little short of quackery, and on the other, the statistical method in medicine as a delusion and fraud. The cause of neither medicine nor statistics is advanced by such amateurish contributions, but a vast amount of harm is done to both medicine and statistics by their publication in scientific periodicals, official health reports, or in the medical press.

Cancer Mortality—Uruguay

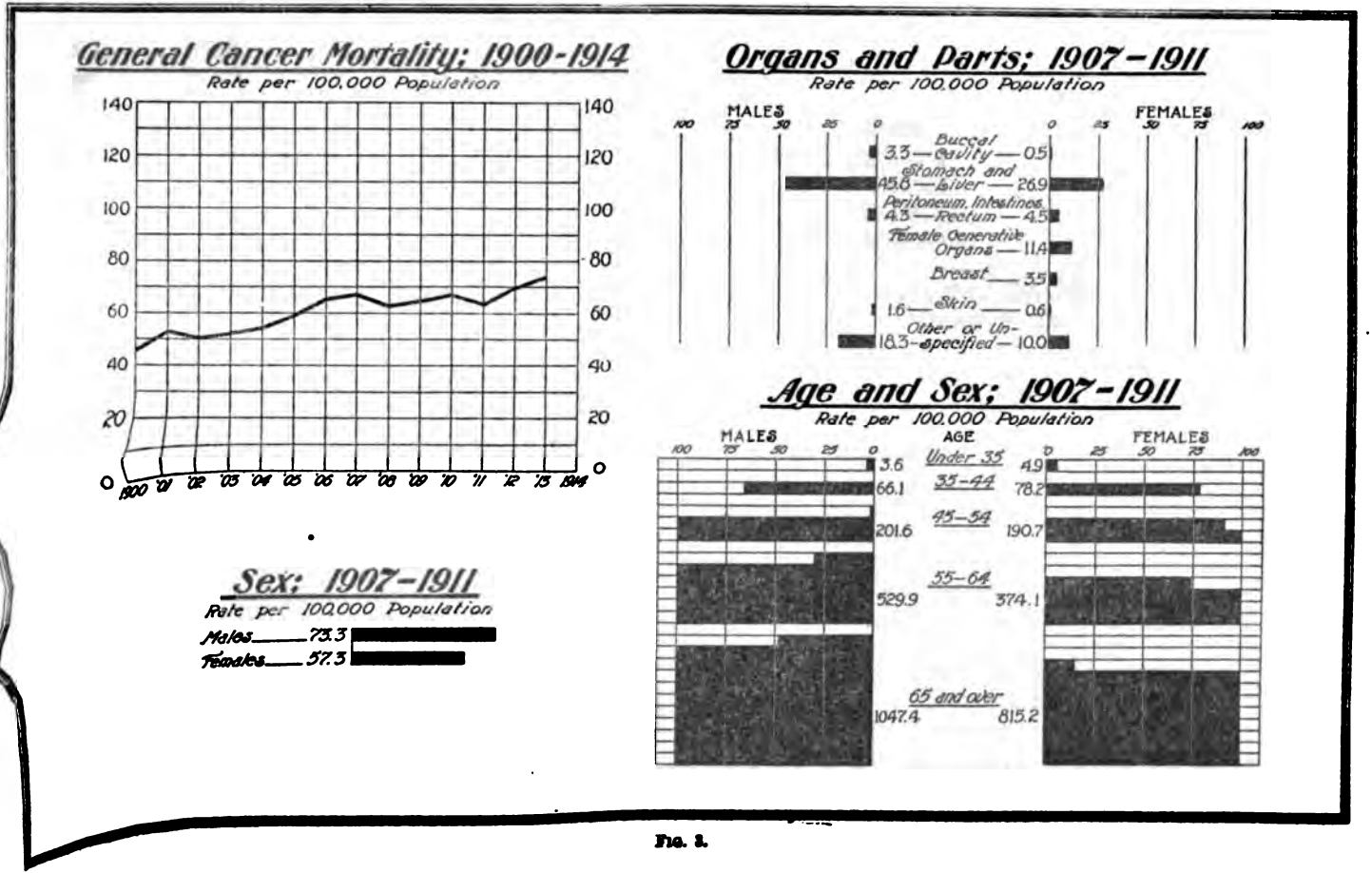


FIG. 8.

Cancer Mortality by Organs and Parts, 1908—1912

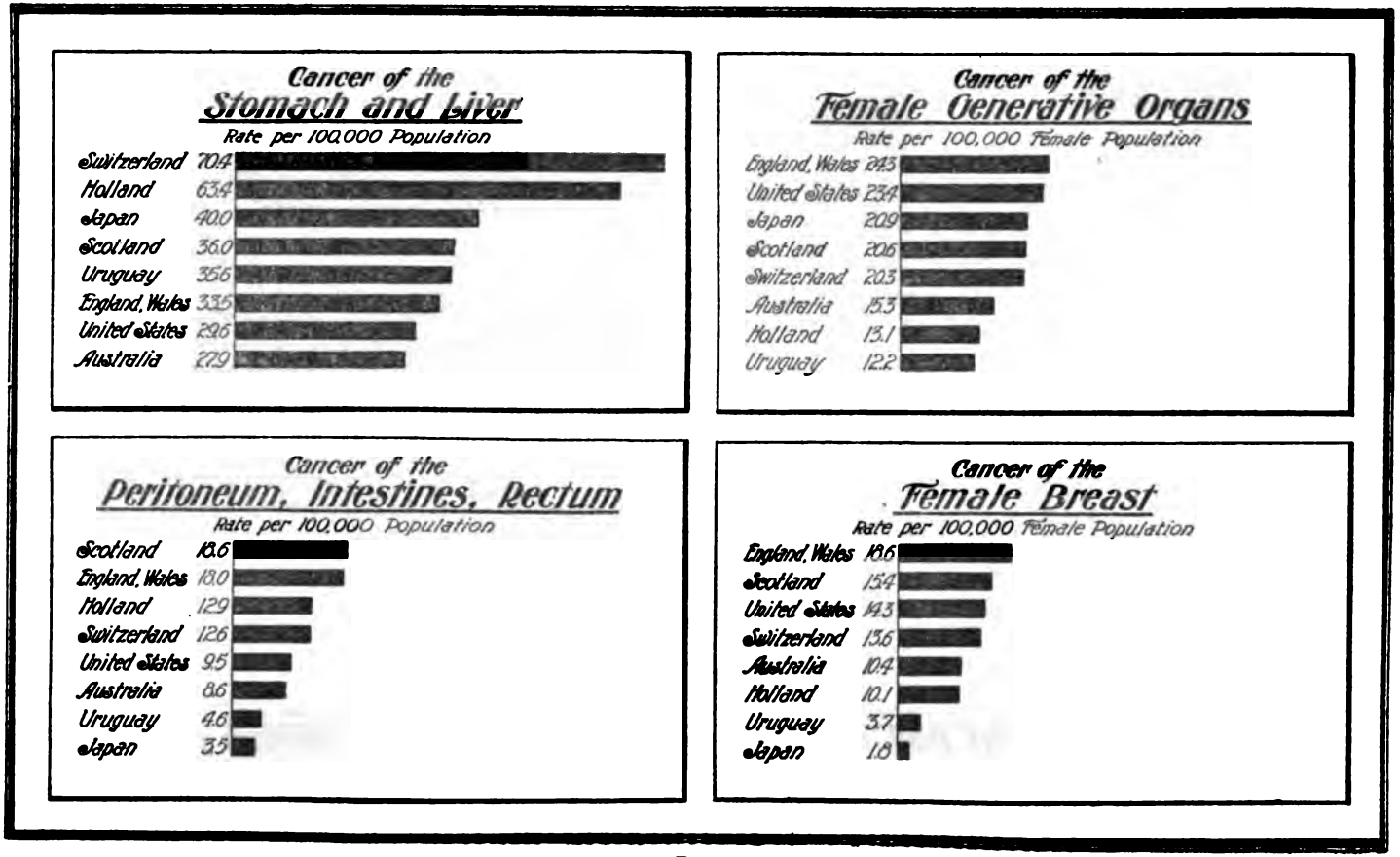


FIG. 4.

URGENCY OF QUALIFIED STATISTICAL RESEARCH.

The foregoing observations are chiefly intended to emphasize the urgency and practical utility of further statistical research into the geographical incidence of cancer throughout the Western Hemisphere. Conceding the rather doubtful accuracy and completeness of the returns for certain countries and islands largely inhabited by native races, it nevertheless seems reasonable to maintain that if malignant disease were actually as common in these areas as in the more civilized portions of the globe, the recorded rate of frequency would be much higher than is actually the case. Recalling the wide disparity in the comparative rate of incidence, by organs and parts, met with in such cities as New York and San Francisco, or Chicago and New Orleans, it would seem utterly incredible that these differences should be the result of serious errors in diagnosis or inaccuracies in death certification, instead of, as is more probable, due to pronounced variations in the existing conditions of life, chiefly habits and diet, which in part at least are the equivalent of material well-being and poverty. While cancer occurs among animals under domestication, or under exceptional laboratory conditions, it is well known that malignant disease is relatively infrequent among wild animals in captivity. Conversely, there are no reasons why native races should be peculiarly or exceptionally liable to malignant disease, and, as a matter of fact, the most careful medical observers, living for many years among primitive peoples, have invariably reported cancer to be of comparatively rare occurrence among them. There are, therefore, convincing reasons for believing that a thoroughly specialized statistical cancer research into the precise geographical incidence of malignant disease throughout the Western Hemisphere would prove of much practical value and possibly of far-reaching importance to the cause of cancer control.

In contrast to the comparative rarity of cancer in many of the countries and islands of Central and South America, the discussion draws attention to the excessive frequency of the disease in such cities as Buenos Aires and Montevideo, where it has been shown that cancer is even more common than in cities of corresponding size in the northern portion of the Western Hemisphere. In this direction also the outlook is encouraging that further statistical research, amplified by medical and anthropological studies, and most of all by thoroughly qualified studies of metabolism diet and habits of life, would yield results of considerable practical importance. Accepting as conclusive the recorded rate of excessive cancer frequency for many of the countries and States of the Pan American Union, it would furthermore seem of the utmost urgency that the attention of these countries should be directed to the principles and methods of the American Society for the Control of Cancer, as a first step in the direction of an effective public education in the essential cancer facts and a prerequisite for an ultimate reduction in the mortality from malignant disease throughout the entire Western Hemisphere.

The CHAIRMAN. The paper just read is open for discussion.

Dr. WILLIAM RODMAN. I was very much struck with one statement that Dr. Hoffman made, which is that malignant disease is certainly more frequent in the fleshy than in those who are under weight. I think there can be no doubt about this. Particularly is this so in patients with cancer of the breast. Some of the statistics that the writer quoted from South American cities rather surprised and startled me.

Dr. TRUMAN ABBE. The paper that Dr. Hoffman has read is extremely interesting and brought to my mind very forcibly the paper that we heard two days ago by Dr. Maud Slye on heredity of cancer in mice. It occurred to me that these factors which influence the

incidence of cancer in particular organs, in various portions of the body, would be fully explained by her proof that cancer is definitely hereditary, not only the tendency to cancer, but the tendency of cancer to special organs. This would account for the increased frequency of cancer of the special organs and the increased frequency of cancer in certain localities. I would like to ask what Dr. Hoffman has to say on that question.

The point as to the prevalence of cancer in people of overweight is a proposition which is, again, very interesting to me, because I have been convinced that in a certain number of cases the overweight is a symptom of the cancer and not the cause of the cancer. It is perfectly true that a large number of the cancer cases that we operate upon and do not cure gain remarkably in weight before a recurrence appears. The same thing is probably true in the early stages of our cancer development, and I was wondering if that would not perhaps account for the overweight suggestion of Dr. Hoffman.

The CHAIRMAN. Dr. Hoffman, will you close the discussion?

Dr. HOFFMAN. The question of overweight in relation to organs and parts has not been statistically studied so far as I know. It is a line of study that I hope myself to take up in the near future in cooperation with the advisory board of the statistical committee of the American Society for the Control of Cancer and the cooperation of some of the leading life-insurance companies in this country, who will be requested to concentrate their attention upon cancer of the breast in women and cancer of the tongue in men. I may state, however, that according to the best information which I have been able to obtain from medical sources cancer occurs more in those who have always enjoyed robust good health, those who represented apparently a better physical type, as measured by an excess in nourishment. As to whether overweight is a symptom, I am not so sure. Miss Attley in Philadelphia has made some extremely interesting investigations regarding weight in relation to cancer of the uterus, and her conclusions were to the effect that a loss in weight had been the earlier symptom of cancer of the generative organs; but her control cases—that is, nonuterine cases—seemed to prove the opposite. I question whether any data at present available permit of a categoric answer to that important question; but it suggests a line of future statistical inquiry which will differentiate the organs and parts and possibly the forms and types of cancer. No progress was made in the study of malaria until fevers were resolved into their different types.

As regards heredity I regret to say that I have been constrained to take an opposite view to that of Miss Maud Slye and her conclusions based upon animal experimentations alone. In her series of charts the other night she had just two family records of human

cancer cases. The collective experience of all American life insurance companies and our own individual company is to the effect that persons with a double history of cancer in the family have slightly lesser mortality from all causes and from cancer in particular than the expected according to age and sex distribution. That is positive evidence, which can not be impeached by the possible doubtful character of the data. A negative statement might be impeached, but these are the facts, that among those who had authenticated cases of cancer in the family, at least two or more, the frequency of cancer in the offspring was less than the expected; so that the evidence of hereditary transmission was disposed of.

The CHAIRMAN. The next paper on the program is "The relation of modes of infection to the control of bacterial diseases in Pan America," by Prof. M. J. Rosenau. Dr. Rosenau has sent his paper with the suggestion that it be read by Mr. Bowles.

THE RELATION OF MODES OF INFECTION TO THE CONTROL OF BACTERIAL DISEASES IN PAN AMERICA.

By M. J. ROSENAU, M. D.,

Professor of Preventive Medicine and Hygiene, Harvard Medical School; Director, School for Health Officers of Harvard-Technology; formerly Director, Hygienic Laboratory, United States Public Health Service, Washington.

Disease knows no geographical boundaries. Germs take no heed of nationality or race. The communicable diseases travel along the routes of human intercourse. Contagion accompanies trade and travel. In the vast majority of instances infection is dragged from one country to another in persons rather than on things. In other words, human intercourse, which brings so many beneficent blessings. also carries in its wake a trail of dangers. These dangers are no less real because they are insidious and due to an invisible foe. Many more persons in the world's history have died of bacteria than of bullets. The encouraging feature is the message of hope found in our knowledge of bacterial diseases, their modes of spread, and means of prevention.

Intercourse between the Pan American States is growing and is bound to increase in volume and in intimacy. With this interchange of products and people will come a corresponding interchange of infections. Fortunately, our methods of quarantine and sanitation have reached that point of precision where we can guard against the introduction of most exotic plagues. Quarantine, however, is only a makeshift and is not the true method of prevention. Quarantine, in fact, is an admission of imperfect sanitation. A city free of Stegomyia mosquitoes can laugh at yellow fever and needs no quarantine. A city with a clean water supply, well protected, need fear no waterborne outbreak of typhoid fever or cholera. A city built with regard to rats will not become an epidemic focus of plague. The "city beautiful" must be the "city clean."

I speak now more particularly of typhoid fever, plague, and cholera, because these diseases represent the types of bacterial infections which are readily controllable. In fact, they are comparatively easy to prevent; impossible to cure.

Typhoid fever is an index of imperfect civilization. A community with a clean drinking water and safe milk supply, a good system of sewage disposal, and otherwise biologically clean, need fear no epidemic of typhoid fever. One of the greatest sanitary triumphs in the history of the world is the remarkable reduction in typhoid fever in the United States during the past decade. Great Plague spots, like Pitts-

burgh and Niagara Falls, which served as endemic foci from which the disease radiated to all parts of our country, at last have been eliminated. Many of the cities and States in our fair land now equal the best records of European cities so far as typhoid death rates are concerned. The period of incubation of typhoid fever is often prolonged—sometimes three weeks or more. A person may thus drink a glass of infected water or contaminated milk in the United States and travel to Brazil, Argentine Republic, or Chile before the disease breaks out. Quarantine procedures are ineffective against typhoid fever, and therefore our reliance must be placed upon the resources of sanitation and personal hygiene.

The brilliant results obtained in the United States Army, through the use of typhoid vaccines, has proved that this is a useful method of prevention. This method of typhoid prophylaxis is also available to the civil population, but does not take the place of hygiene and sanitation.

The story of cholera is an exact counterpart of that of typhoid fever. Cholera is spread in precisely the same way that typhoid fever is spread, and bacillus carriers play the same insidious roll in both diseases. "Flies, fingers, and filth" are illiterative truths in both infections. Furthermore, it is literally true in both cholera and typhoid fever that "disease, dirt, and diarrhea" become sadly mixed.

Bubonic plague has found a foothold on the American Continent and will be difficult to eradicate. Plague is a bacterial disease, but is an exception to the rule in that it is spread not so much from person to person as through the intermediary of the rat and its flea. Plague is a disease, primarially, of rats and secondarily of man. This exotic pestilence is dragged from country to country mainly by the rats on board ships. Quarantine restrictions against plague are effective but cumbersome to trade and travel. A rat-free city could lighten the delays and expense of quarantine measures against plague.

Nations must learn the lesson that it will pay to require rat-proof buildings, rat-proof markets, wharves, graneries, and slaughterhouses, just as it has found by bitter experience that it pays to have other restrictive building laws.

Monumental public buildings, beautiful parks, art galleries, libraries, and handsome boulevards do not make the "city beautiful." The sanitarian looks deeper than these outward expressions of prosperity and appreciation of fine arts. He requires a clean city in the sense of biological cleanliness—free of rats, flees, vermin, and dust; good houses, clean from garret to cellar; tidy back yards—in fact, cleanliness of the food we eat, water we drink, air we breathe. Cleanliness of home and surroundings is the foundation stone of an enduring structure in preventive medicine. The greatest blessing to man is health, and this can not be achieved without intelligent effort and the expenditure of time and money. "The healthy man is the most meritorious product of nature as far as he goes. A soul in right health is the blessedest thing this earth receives of heaven."

The CHAIRMAN. This paper is now open for discussion.

Mr. JAMES T. B. BOWLES. I had the pleasure of serving in Panama for nearly six years. My mind goes back to the nidus of the infections which were formed by trade routes, beginning at the old town of Portobelo. Sailing vessels first stopped at Portobelo, as there were markets and fairs there. Cargo and passengers were then transferred to small sailing vessels for the village of Chagres, which in turn became a new center of infection for yellow fever and malaria, and so it continued. Each one of the places along the trade route became a center of infection for yellow fever and malaria, and as these routes were traveled by the people crossing Panama the centers of infection were kept up by the new blood passing through.

The point was brought out that quarantine is only a makeshift and is not a true method of prevention. I think this is very well illustrated by the conditions in Panama. With the present sanitary conditions there, quarantine would not be necessary if it were not for the conditions of some of the places lower down in South America. That is easily seen from the fact that occasionally it has been necessary to strengthen the quarantine regulations at the port of Panama City.

Dr. Rosenau places a great deal of stress on typhoid fever. The control of typhoid fever in Panama is another wonderful thing. I know of practically only two very small outbreaks of typhoid fever. There were a few cases at two different times. The first few cases were practically water borne through a water carrier who had been infected with typhoid fever. The second series of cases occurred two or three years ago, through the infection of the oyster beds in the bay by the sewerage of Panama City. There were only a very few cases then. I think we can say that the death rate in Panama from typhoid is practically nil, far less than in any of the American cities.

The typhoid death rate in the Army was very interestingly brought out. Last year when we were in Vera Cruz we did not have one case of typhoid fever in the Army. This certainly vindicates the prophylactic use of vaccination against typhoid fever. When we went into Vera Cruz we found a great deal of typhoid and tuberculosis there.

The CHAIRMAN. It is perfectly true that to have a city in such sanitary condition that a disease can not spread is infinitely better than a measure to keep it out. At the same time the economic question plays its rôle even in sanitary affairs. Sometimes a dollar will do more in keeping disease out than a good many dollars will in preventing its spread, and if you can keep it out, as a makeshift at least, it is very well to do so.

The next paper on the program is that of Prof. S. J. Meltzer, Rockefeller Institute, New York City.

ON THE INHIBITORY PROPERTIES OF MAGNESIUM SULPHATE AND THEIR THERAPEUTIC APPLICATION IN TETANUS.

By S. J. MELTZER.

Department of Physiology and Pharmacology of the Rockefeller Institute for Medical Research, New York.

INTRODUCTION.

The object of my communication is chiefly a practical one. I wish to state in a precise way how magnesium sulphate should be used in the treatment of tetanus. It is not improbable that there are many in this audience who know that this salt is being used for treatment of tetanus, but I doubt that many are familiar with the pharmacological

action of this salt upon which this method of treatment is based. It is conceivable that it is assumed by many that any favorable therapeutic effect Epsom salt may exert upon tetanus rests upon its well-known action as a purgative. Furthermore, I can not free myself from the doubt that the physiological phenomenon of inhibition is generally well understood, and especially that the term "inhibitory property," which has been used in the title of this paper in connection with the action of magnesium salts, will be properly interpreted. My practical statements will, therefore, have to be introduced by a discussion of a theoretical character. In this discussion I shall deal briefly, first, with the phenomena of inhibition, as I understand them, and then proceed to discuss the inhibitory actions of the salts of magnesium which we observed in our experimental studies and which led up to the use of magnesium sulphate in tetanus.

THE PHENOMENA OF INHIBITION IN BIOLOGY.

The best known phenomenon of inhibition is the action of the vagus upon the heart. The heart is a muscle which continually performs rhythmical contractions. When a nerve which goes to a muscle is stimulated, the muscle gets into a shorter or longer state of tetanus. But the Weber brothers discovered that stimulation of the peripheral end of the vagus nerve stops the heart in diastole—it inhibits its contraction. The phenomenon of inhibition was thus discovered. In the past 70 years a great many physiological processes were discovered which had to be interpreted as inhibitory phenomena. I shall not attempt to discuss here the great amount of the corresponding data, which, by the way, have not yet been sufficiently correlated. I shall only discuss two or three points which are very useful to keep in mind. Many years after the vagus inhibition came to light, nerve fibers were discovered, the stimulation of which causes an acceleration of the heart beats; it was further established that when the inhibitory vagus fibers and the accelerator nerve fibers are stimulated simultaneously, the effect of inhibition prevails during stimulation to a degree that the stimulation of the accelerators can not be well recognized. But both sets of nerve fibers differ in some peculiarities, among others, in the fact that stimulation of the accelerator nerves leaves a long after effect, while the inhibitory nerve fibers of the vagus manifest only a short after effect. This leads to the result that when both sets of fibers are stimulated simultaneously a considerable acceleration of the heart beat follows soon after discontinuation of the stimulation. By this phenomenon the presence of accelerators, or, as it is also termed, augmenting nerve fibers in a nerve trunk are recognized. In other functions opposite relations prevail, namely, the augmentors predominate during stimulation and the inhibitors possess the longer after effect.

It is readily conceivable that the effect of stimulation of a single nerve trunk could be interpreted in various ways, which, of course, I should not analyze here. I need only to add that the above-mentioned antagonism applies not only to the motor sphere, but is readily adaptable also to the functions of secretion and sensation and, furthermore, is applicable also to functions in which the augmenting and inhibitory processes are not represented by well-defined nerves or other morphological units.

It is very useful to have another consideration well fixed in mind. By our daily habits we are used to the mode of thinking that any action, a motion, or a secretion, is brought about by a positive cause, a definite stimulus. The absence of such an action seems not to need any explanation; a thing, for instance, does not move simply because there is no cause for its motion. This, however, is not true even in the inorganic physical world. A thing does not move in a certain direction merely because it is prevented by an opposing force of exactly similar energy which works in an exactly opposing direction. By an analysis of numerous living phenomena I came to the conclusion that all living functions are continually controlled by two opposing forces—augmentation or action on the one hand and inhibition on the other hand. The state of every function at every moment depends upon the relation and the predominance of each of these opposing functions. Taking motion as an

instance, the maximum effect of the action factor in a living body is tetanus, and the maximum effect of inhibition is complete relaxation. The various degrees of tonus present an intermediary state in which one of the opposing forces is more or less predominating. Some forms of absolute paralysis may not present life phenomena; they may have been brought about, indeed, by the absence of a living cause. For several decades this theory, and especially the notion that inhibition is a most extensive factor in all manifestations of life, played a dominating part in all my researches and was a working factor in my investigations of the physiological functions of deglutition and of respiration.

THE INHIBITORY ACTION OF MAGNESIUM SALTS.

Some 19 years ago I studied the effect of intracerebral injection of small quantities of various salts. While the effect of nearly every kind of salt consisted in the causation of a more or less intense and characteristic convulsive attack, I found that after an intracerebral injection of a few drops of a 5 per cent magnesium sulphate solution the animal turned on one side and remained for hours in a stuporous condition. Under the influence of the conception that inhibition is an important factor in the functions of the living body the question arose in my mind whether a definite relation exists between the magnesium ion in the body and its various states of inhibition or depression. A review of the literature revealed that the action of magnesium salts had been very little and only superficially studied. The same may be said of the researches concerning the phenomena of inhibition; the various degrees of depression in the various functional activities were rarely united in a single general point of view. It was mostly the various forms of excitation (action) which fascinated the attention of the physiologist and were investigated as a problem of irritability. On the basis of the above-formulated question we investigated in the last dozen of years in the department of physiology and pharmacology at the Rockefeller Institute with Dr. John Auer and other associates the various actions of magnesium upon the animal body. After a long experience we may say to-day that the dominant action of magnesium salts upon the living body, no matter by which way it is administered, is that of *depression* or inhibition.

We shall, of course, not enter here upon many details, but shall mention a few facts very briefly. When after the administration of a very small amount of ether, insufficient to cause anasthesia. an ine ficient amount of magnesium sulphate is injected intramuscularly, a profound anasthesia follows which can be maintained for several hours. Consciousness is the first thing completely abolished, the unconsciousness being, as a rule, accompanied by a great muscular relaxation, while all the reflexes remain nearly unaffected. With a larger dose of magnesium the reflexes, too, are gone, and with a still further increase of the magnesium dose the motor nerve endings become paralyzed—a curare like action—accompanied, of course, by a simultaneous profound central action. This was obesrved in a number of operations performed upon human beings by Dr. Peck and also in some cases of Dr. Elsberg.

Chemically calcium and magnesium are closely related substances. Biologically, however, they are strikingly antagonistic to one another. Auer and I found that an animal which may have been completely paralyzed by a magnesium salt can be restored within a fraction of a minute by an intravenous injection of a calcium salt. This, however, applies essentially to conditions in which the animal was exposed to the effect of magnesium for a comparatively short time. When the animal is saturated with magnesium for a longer period the antagonistic action of calcium is less evident and is not even without some danger.

At the last meeting of the International Physiological Congress in Groningen (1913) I offered the following hypothesis in explanation of the mentioned phenomena. As it is well known the various neurons are connected by mere contact, which is termed by Sherrington "synaptic membrane." The connection between motor nerve

and muscle is also not of a very solid character and is termed by some also as synaptic membrane. My theory assumes that the magnesium contained in the lymph which bathes the synaptic membrane enters with ease into these spaces and interrupts the passage of such impulses which have a less readily prepared path than reflexes for their transmission from neurone to neurone. Again, the synaptic membrane between two neurons offers less resistance to the entrance of the magnesium than the more solid membrane between the motor nerve and the muscle. The same applies to the calcium. When it is present in the lymph in a quantity larger than normal it enters readily into the synaptic membrane and displaces or neutralizes there the obstructing or inhibiting magnesium. When, however, the magnesium, by its long-lasting presence, manages in some way to enter into the inside of a nerve cell, the calcium is incapable to dislodge or neutralize there the magnesium readily. This theoretical view may have some bearing upon the mode of the therapeutic action of magnesium salts in tetanus.

THE TREATMENT OF TETANUS BY MAGNESIUM SULPHATE.

The effect of magnesium salts was investigated extensively on animals and in a comparatively moderate degree on human beings by different modes of administration—by intravenous, intraspinal, intramuscular, and subcutaneous injections. In all modes of administration the character of the effect is, as stated before, unmistakably depressing in character. In intravenous application the effect is rapid, but is comparatively of short duration and it must be guarded against possible harmful incidents. The inhibitory effect of an intraspinal injection sets in fairly early and may last even longer than 24 hours. Intramuscular injections have a fairly early effect, but are only of a comparatively short duration. Subcutaneous injections act slowly, but have a cumulative action.[1]

I shall deal here exclusively with the favorable action of magnesium sulphate upon tetanus. The action may appear to some as a merely symptomatic one; it relieves the convulsions. But even if this would be indeed its only favorable effect, it would be of unestimable value, since the suffering in tetanus and the fatal outcome of this horrible disease is nearly exclusively due to the consequences of the tetanic symptoms. And we may claim that there is no other remedy which is capable of relieving the furious symptoms to such a satisfactory degree as the injection of magnesium sulphate. But on the basis of the above-mentioned theory, we may expect from the use of magnesium sulphate perhaps even more than a symptomatic action. It is possible that the magnesium salts, accumulated in the lymph, enter into the synaptic membrane between two nuerons and thus prevent the wandering of the tetanus toxin into higher neurones and the corresponding nerve cells.

Soon after our publications on the inhibitory action of magnesium salts clinical cases of tetanus began to appear in the medical literature in which magnesium sulphate was used. This was especially the case after the favorable report published by the famous surgeon, Theodor Kocher, of Berne. At the outbreak of war numerous cases of tetanus were treated by magnesium sulphate. I shall not enter here upon an analysis of the extensive literature on that subject. I wish only to say that a study of this literature convinced me that in many instances the writers were neither familiar with the pharmacological principles underlying this treatment nor with its indications or contraindications, and some of the conclusions which they derive from their observations were hastily drawn and without proper criticism. Some did not know enough to distinguish between the symptoms due to the disease and those which were brought about by an improper use of the magnesium salts.

In the following I shall try to lay down some rules for the use of magnesium sulphate in tetanus as I learned them from our extensive experimental investigations and

[1] Also local application exerts unmistakably some favorable effect upon burns, erysipelas, etc., but I shall not deal here with this side of the subject.

from an unbiased, critical study of the clinical literature of that subject. However, in employing magnesium sulphate for the treatment of tetanus and in drawing conclusions from such observations there are a few things which one has to keep in mind and to which I wish to call attention before I proceed to describe the methods to be used, their respective advantages and disadvantages, and the procedures which are necessary to meet the latter.

There are advanced and dangerous forms of tetanus which can not be cured, or even relieved temporarily, by any method of treatment; the failure of magnesium in such cases should in no way militate against the possible usefulness of this method. The treatment of tetanus by magnesium does in no way preclude a simultaneous treatment with antitetanic serum. The suffering of tetanic patients is too great and the outlook is too grave to permit the experimental method of treatment—i. e., to test one remedy at one time. Even if magnesium sulphate would do no more than relieve the most severe symptoms, the convulsions and the tetanus, it would be a duty to use it. If properly used it is certainly capable of reliably relieving severe symptoms in many cases better than by any other remedy. It is necessary to know the possible dangers which may be brought about by the use of magnesium salts; at the same time it is necessary to know well the incidents of tetanus, in order not to look upon them as effects of the magnesium injection. This confusion occurred in many instances. Magnesium may bring about a temporary reversible paralysis of the respiration. We shall discuss later how to avoid this incident and how to meet it when it occurs. The circulation is not readily affected by the injection of the magnesium salt and such an an incident ought never to occur. Magnesium salts cause a temporary appearance of hyaline casts in the urine (Peck, Gates) which disappear readily and early; nevertheless magnesium injections should not be used in cases of outspoken nephritis. Intravenous injections of magnesium salt causes a definite hyperglycemia, with only a mild glycosuria (Kleiner and Meltzer). It is, however, a merely temporary phenomenon and is no contraindication to the use of magnesium salts.

We shall now proceed to a description of methods of administration of magnesium salts in tetanus.

1. *Intraspinal injection.*—It may be stated that for adults this method of administration gives the best results. The sulphate of magnesium (Epsom salt, $MgSO_4+7H_2O$) should be administered in a 25 per cent solution, 1 cubic centimeter of the solution to each 20 pounds of body weight. In cases of strong opisthotonus it is advisable that the injection be preceded by a moderate general anesthesia, ether, or chloroform, which should be discontinued immediately after the injection is completed. The injection should be made in the lumbar region at the usual place and with the usual precautions. The patient should then be placed on the back. The relief may begin to become manifest in a short time after the injection, and leads, as a rule, to a complete relaxation lasting 24 hours and longer. During this period the patient is resting, relieved, partakes of food, and may fall into a deep sleep. Sooner or later, however, stiffness and convulsive seizures will return. A second injection ought to be given before the tetanic conditions attain their original intensity. The second dose, however, ought to be smaller, for instance, about 0.8 cubic centimeter per 20 pounds. The repeated injections ought to be adapted to the conditions of the patient, which mostly do not demand a complete relaxation. It may be necessary to catheterize the patient. This and the occasional rise of termperature do not present contraindications to this method of treatment. The only serious phenomenon which may complicate this procedure is the setting in of a weakening or a temporary standstill of the respiration due undoubtedly to a paralysis of the respiratory center by the magnesium. As a rule, when the above-described procedure is followed out carefully, this serious incident does not occur in adults. It is, however, well to know how to proceed when this complication makes its appearance. A needle should be introduced into the lumbar canal, through which some of the spinal fluid should be permitted to run out, and then the cana

washed out several times with a Ringer solution. During this procedure the upper part of the body should be kept elevated, to facilitate the escape of the fluid from the spinal canal; also artificial respiration should be instituted with air or oxygen, for both of which my apparatus of pharyngeal insufflation which I describe elsewhere is the most suitable one.

Both the washing of the canal and the artificial respiration should be instituted at an early stage; that is, as soon as the respiration becomes slow and shallow. The recovery will follow rapidly. Action should not be delayed until the respiration actually ceases; the preceding prolonged asphyxia may be a hindrance to the prompt recovery. The use of calcium or physostigmin, which we shall mention in describing the other methods of application, are of no avail in the intraspinal method. As stated before, the occurrence of a respiratory complication is not to be feared when used in adults according to prescribed rules. In very young children the initial dose should not be higher than 0.5 cubic centimeter of a 25 per cent solution per 20 pounds. For the present it is perhaps better not to use it as a routine method in children. The intracommunication between the various sections of the intraspinal canal is probably much freer in very young children than in adults.

2. *Subcutaneous injection.*—This method is incapable of relieving severe acute attacks of tetanic conditions unless used in immense doses. On the other hand, small doses used three or four times a day undoubtedly gradually reduce the increased irritability and may lead even in severe cases to a final recovery. The dose should be for adults about 1.2 cubic centimeters and for children 0.6 to 0.8 centimeter per kilogram of body weight of a 25 per cent solution three to four times a day. It should be begun as soon as symptoms of a local tetanus (drawing of the muscles in a slightly wounded extremity, slight difficulty in swallowing, slight trismus, etc.) make their appearance and be continued until all tetanic symptoms disappear. The use of a moderate local or general anesthetic facilitates these injections, which should be made under the necessary aseptic or antiseptic precautions. It should be borne in mind that such injections are incapable of offering a rapid relief in acute tetanic attacks and their value should not be discredited by their failure to relieve satisfactorily acute dangerous seizures.

3. *Intravenous injection.*—Magnesium salts disappear rapidly from the circulation; this method is therefore inappropriate for the purpose of bringing about a complete cure; besides, under prolonged use it may act unfavorably upon the circulation. In a previous communication I advised against its use. However, after a series of experiments with Dr. Auer on tetanic dogs and after the clinical communications of Hans Kohn and of Walter Straub, I became convinced that this method, if used properly, may save life in severe dangerous tetanic attacks of the pharynx, the larynx, or the diaphragm. It should be used in a 6 per cent solution 2 to 3 cubic centimeters per minute, and it should be discontinued immediately as soon as the respiration becomes shallow. As a rule, the respiration improves soon after the infusion of magnesium is discontinued. If the improvement is not prompt enough a small amount of $CaCl_2$ (2.5 per cent) should be slowly injected through the venous cannula, used for the infusion of magnesium, until the respiration shows a definite improvement, which may appear in less than 30 seconds. The calcium injection should be immediately discontinued; otherwise all the previous tetanic manifestations may make their reappearance. The striking favorable effects of intravenous injections of magnesium may disappear in 30 to 40 minutes, but the actual dangerous symptoms may be obviated for a much longer period.

4. *Intramuscular injection plus ether inhalation.*—In experiments of Auer and the writer it was established that an injection of only 2.4 cubic centimeters of a 25 per cent solution of magnesium sulphate, given intramuscularly combined with a temporary mild ether inhalation, is capable of bringing about a considerable relief in less than half an hour, and may last for several hours. The method is inappropriate for frequent repetitions.

Should it by unforeseen accident be found that during the use of one of the three last-mentioned methods the respiration became affected, an intramuscular injection of a 2.5 per cent solution of 2.5 per cent solution of $CaCl^2$ may slowly neutralize the unfavorable respiratory effect without bringing back serious tetanic symptoms. An injection of about 1 milligram of physostigmin is also capable of improving the respiration.

Summary—The best general plan for treatment of tetanus would seem to be as follows: To give in each and every case of tetanus by subcutaneous injection 1.2 cubic centimeters of a 25 per cent solution of magnesium sulphate per kilo body weight three times a day throughout the entire disease. When the disease is complicated with severe tetanic attacks, to give (in adults) by the intraspinal method 1 cubic centimeter of a 25 per cent solution for every 10 kilograms (20 pounds) body weight. When the disease is attended by immediately dangerous tetanic complications, to give by intravenous injection 2 to 3 cubic centimeters per minute of a 6 per cent solution of magnesium salts until the dangerous symptoms subside, or the respiration becomes shallow and too slow. When the respiration seems to become impaired in consequence of the use of the magnesium salt by the way of circulatory apparatus, to inject intramuscularly 10 to 15 cubic centimeters of a 2.5 per cent solution of calcium chloride. It is advisable to have at hand an apparatus of intrapharyngeal insufflation, ready for use whenever the respiration becomes slow and shallow. Finally, not to neglect the simultaneous treatment with serum.

Dr. BAYER. I was present about 19 years ago at a meeting of the American Physiological Association in New Haven when Dr. Meltzer demonstrated for the first time the effect of intracranial injections of the several salts which he has mentioned, among which were magnesium chloride, sodium chloride, and potassium salts. We were very much surprised, but it meant only a very curious and as yet unexplained phenomenon, and it is due to the fertile mind of Dr. Meltzer and a few special students that there has been carried on the study of their peculiar and most important effect on the nervous system. It happened to be my fortune to be in Germany at the outbreak of the war, and my further good fortune to assist one of the famous surgeons in Germany during the first eight months of the war. We had our usual number of tetanus cases, which did not respond to any treatment that we could devise. Some of these days I hope that we may save our patients that are now dying of tetanus by the improved method which Dr. Meltzer gives.

Dr. BROWN. I should like to ask Dr. Meltzer whether the local injection of a solution of magnesium sulphate has any effect upon the destruction of the tetanus toxin from its location—that is, near the place of injury.

Dr. HOUGHTON. I would like to ask Dr. Meltzer if he has any considerable data showing the comparative results upon animals treated with antitetanic serum by itself and by the combined method. I have been very much interested in the development of the use of magnesium sulphate, so much so that two or three years ago I had conducted in my laboratory a series of experiments upon sheep, for the purpose of finding out how much value could be attributed to

the various kinds of treatment proposed. While I can not give definitely the data—I have not gone over it lately—we found that the use of magnesium sulphate did not show a diminution in the amount of tetanus toxin that was manifestly present in the blood of the sheep when drawn from the animal after it had developed symptoms of disease and had been treated with magnesium. The same experiments were undertaken with tetanus antitoxin. In each case there was apparently some diminution in the amount of toxin that could be demonstrated present. Ether and trichlortertiary butylalcohol, or chloretone, was also used, but with none of them could we ever firmly establish, with the possible exception of the antitetanic serum, that there was a diminution in the amount of toxin present in the blood.

From this I believe the conclusion might be drawn that the use of magnesium sulphate, the use of trichlortertiary butylalcohol, chloral, or any other anesthetic of that series, merely assists in the control of the symptoms manifested by the animals. As a result of our studies, which covered a considerable length of time on many animals, we arrived at the conclusion that the best method of treating tetanus in the lower animals was through the use of antitetanic serum combined with the use of an anesthetic, either chloroform, ether, or trichlortertiary butylalcohol. It was rather gratifying to note in a recent number of the Lancet quite a lengthy article by one of the English surgeons in which he discussed various methods of treatment, and gave in the conclusion of his article what he believed to be the best method of treatment. This corresponded very closely to the treatment we had determined experimentally in the laboratory, viz, the use of an anesthetic with the antitetanic serum. About the same time I received a communication from Prof. Sims Woodward, a private communication (as you know, he is professor of pathology in the University of Cambridge, England), in which he congratulated the medical profession, particularly the bacteriologists, for having been able to devise and elaborate a product—antitetanic serum—which had so nearly robbed war of the terrible scourge of tetanus.

The CHAIRMAN. Is there any further discussion? If not, Prof. Meltzer will close.

Dr. MELTZER. Dr. Bayer, I think, was in Hamburg. They did not use there the magnesium sulphate, although they had used it extensively in other places on the German side where there were enormous numbers of cases of tetanus at the beginning of the war.

In regard to the question of Dr. Brown, whether the injection of magnesium has any direct effect upon the tetanus toxin, I would answer negatively.

As to Dr. Houghton, I am familiar with that article which came out from the Parke-Davis Laboratory. After the effect of magnesium be-

came known, this laboratory recommended also chloretone which is manufactured there. They used intraperitoneal injections and I am sure that they were not justified in drawing the conclusions they have.

Now, does magnesium have any effect upon the toxin? We do not mean to influence the tetanus toxin. Then, as to the experimental work on animals, I can say that the only sure animal on which you can make experiments by intraspinal injection is the monkey. We never succeeded in doing anything by intraspinal injection in other animals.

The CHAIRMAN. The next paper is by Dr. R. González-Rincones, of Venezuela, on "Tropical parasitosis."

OBSERVACIONES SOBRE PARÁSITOS TROPICALES.

Por RAFAEL GONZÁLEZ-RINCONES,
Profesor de la Facultad de Medicina de Caracas, Venezuela.

Ascaridiosis.—El Dr. Ascanio, de Caracas, ha tenido oportunidad de tratar muchos casos de ascaridiosis con la esencia de chenopodium, sólo o asociada a la santonina y al calomel. El Dr. Ascanio atribuye gran importancia al momento en que se administra el vermífugo, basándose en una creencia popular según la cual los resultados más probables son obtenidos tres días antes de que la luna entre en su primera fas mensual y el día antes de que el astro entre en el cuarto menguante.

Anquilostomosis.—Timol y el chenopodium. Leche de higuerote, Novo-timobenzol.

Bilharziosis.—Los primeros casos fueron señalados en Caracas por Rangel y Soto, en noviembre de 1906 (Sch. Mansoni).

El Dr. Elías Rodríguez, de Caracas, aconseja el tratamiento siguiente: Tres pastillas de El Kossam por día y al siguiente, una cápsula de helecho macho, por la noche, al acostarse, tres a cuatro horas después de la última comida. Continuar idéntico tratamiento durante meses, ingiriendo alternativamente, las tres pastillas y la cápsula. Según observaciones del Dr. Ascanio, desde el vigésimo día los huevos de *Bilharzia* desaparecen de las heces; los casos que ha sometido a este sistema durante cinco meses seguidos, parecen estar curados, como autorizan a suponerlo las observaciones clínicas de esos sujetos y los exámenes de heces periódicos practicados durante un año por lapsos de 20 días.

Por mi parte, basándome en la presencia de los parásitos en la vena porta y sus ramas, administro dosis fraccionadas de calomel o protoioduro, bicloruro o bioduro de mercurio. Como la absorción de estas sales se hace por el sistema porta en gran parte donde precisamente viven los vermes, parece racional el empleo del tratamiento mercurial, siempre que se establezca con el mismo cuidado y las mismas precauciones de dosificación que en el tratamiento de la sífilis. Para activar la eliminación, administro de 0.25 a 0.50 gramos de teobromina durante 15 días, al mes de haber iniciado la cura mercurial.

Para combatir la anemia y sostener la acción medicamentosa, administro al tercer mes el licor de Donovan Ferrari. Siempre que me es posible, someto al enfermo a la irradiación de una ampolla de rayos X, para esterilizar los parásitos machos y hembras que se hallan en la vena porta y sus ramas intra hepáticas, basándome en la acción bien conocida que ejercen los rayos X y los rayos [illegible] (beta) del radio sobre los epitelios germinativos. He obtenido ya muy buenos resultados con la irradiación.

La aplicación de los rayos X para el tratamiento de las bilharziosas debe ceñirse a las reglas de la radioterapia profunda; empleo el sistema de fuegos cruzados, sin pasar nunca del tinte II del radio-cromómetro de Bordier.

La emetina no ha dado resultados en esta parasitosis. Tampoco hemos obtenido los resultados que se esperaban con una fórmula que me suministró el Dr. Robinson, por haberle escrito el Dr. Andrew Balfour, de Londres, a su regreso de una expedición por Granada, Barbada, Trinidad, Venezuela y Colombia, que la bilharziosis existía en Venezuela, según pudo verlo en preparaciones que le mostré en mi laboratorio.

Para una cápsula: Timol, 0 gr. 60; benzol, 1 gr. 80.

La administración del timol así disuelto, en 79 casos de bilharziosis, no ha producido nunca ningún accidente tóxico. En un caso el enfermo, tomó durante dos meses consecutivos, dos cápsulas diarias de timo-benzol al acostarse, sin el menor inconveniente.

La fórmula precedente, por la cual doy en esta ocasión las gracias a su autor, Dr. Robinson, a cuya intervención la debo, ha servido de base al Dr. Ascanio para un nuevo tratamiento contra la tenia y el anquilostomo.

El Dr. Ascanio tiene numerosas observaciones de sujetos a quienes ha hecho expulsar sus tenias con una solución de timol en benzol, saturada de alcanfor. Se administra en las condiciones que se exigen para la administración del timol en la anquilostomosis y el resultado es rápido y absolutamente exento de peligro si el medicamento es precedido de un purgante de sulfato de soda y seguido de otro de la misma sal. Las tenias son expulsades en bloques y no parsimoniosamente como sucede con el helecho nacho, cuyos fenómenos tóxicos son demasiado frecuentes en los enfermos a quienes se administre en dosis suficiente.

El Dr. Ascanio usa también la fórmula de Robinson modificada, la cual denomina novo-timo-benzol, en el tratamiento de la anquilostomosis y hace notar que el éxito es seguro y el tratamiento mucho mejor aceptado por los enfermos (cualquiera que sea su estado) que el timol en polvo puro. Cree que la adición del alcanfor modifica la acción irritativa del timol sobre la mucosa gástrica y al mismo tiempo el corazón es tonificado. Ha seguido comparativamente en varios casos, por medio del esfigmo manómetro de Pachon y del esfigmógrafo, la tensión arterial y los trazos esfigmográficos en sujetos diferentes a quienes ha administrado el mismo día los preparados siguientes: timol sólo, en sellos; timol con azúcar, también en sellos; timo-benzol de Robinson y novo-timo-benzol. El Dr. Ascanio considera esta última fórmula como tratamiento de elección en la anquilostomosis y para la expulsión de teniados.

Tricocefalosis.—Los Dres. Fonseca y Ascanio han obtenido buenos resultados con la asociación de la esencia de chenopodium, santonina, calomel y aceite de ricino. Es muy popular el uso de la leche de higuerote morado, contra este parásito. Se administra como en Colombia y Centro América, durante varios días, y luego se purga al enfermo con un salino. Es de lamentarse que no se encuentre todavía este producto bajo una forma comercial de fácil adquisición.

THE CHAIRMAN. Is there any debate upon the paper?

Dr. HALL. The treatment of parasites is being taken up by the United States Bureau of Animal Industry with a view to determining what things are really efficacious. Clinical treatments are often unsatisfactory so far as positive results are concerned. In human parasites we are limited to an examination of the feces, and while fecal examinations are reliable within their limits, there are a number of factors which limit the findings. In the experiments which we have been carrying on we have in all cases followed feces passed for four days. The experiment animal was then used for post mortem. The animal used in most of our series so far has been the dog, which

has a comparatively simple digestive tract. There are certain things which warrant deductions applicable to the case of man, as the parasites found in the dog are themselves rather closely related to those of man. We can confirm in our experiments the statements of Dr. Rincones that oleum chinopodium seems especially efficacious, very frequently having an efficacy of 100 per cent for a single treatment, which is, in our experience with anthelmintic, exceptional. The toxic dose for oleum chinopodium in the case of the dog is 0.6 of a cubic centimeter per kilo weight of dog. We have used it 0.01, 0.02, 0.03 in all cases where repeated doses were bringing it up to the lethal dose, and without injury in most cases to the animal. That is very much in excess of the dose for man, where the dose runs 6 to 10 drops administered three times at hour intervals, and I venture to say that the dose now being used for man could in all probability be safely increased. However, if it seems sufficiently efficacious in its present dose, there would be no object in increasing it, as there is a certain amount of irritation to be expected. Still, chinopodium is in the main a safe drug. It is constipating and demands, of course, a purgative treatment following it. It has this interesting feature—that its administration in oil and the administration of oils following it diminishes the toxicity instead of increasing it, as in the case of male fern and some other drugs.

In the case of hookworms, which have been recently stated to be quite amenable to the action of oleum chinopodium, we have not found its efficacy as great as it is against ascaris. It seems to be only moderately efficacious against the hookworm of the dog, but it has been recorded that in the use of oleum chinopodium in over 100,000 cases of hookworm treatments in various parts of the world it has been found more satisfactory than thymol, more efficacious and less toxic. Lane finds it to be, roughly speaking, 91 per cent in efficaciousness, as I remember the figures, as against 87 for thymol.

Hookworms, in our experience, are removable only by accident, and almost any anthelmintic may be occasionally efficacious against hookworms. It seems to be not a matter of whether a given anthelmintic can kill a hookworm, but a matter of whether a dose of any given anthelmintic will make the journey from the ileocecal valve back to where the hookworm is located.

I have been very much interested in the reports from Central America, where it is stated that they are using various species of ficus that is said to be extremely efficacious against hookworm. I wonder whether in this we have something which can be depended upon to go back into the cecum and get at the hookworm. We know so little about the conditions covering the course of the ingesta from the ileocecal valve—that seems to be a subject upon which we have

comparatively little data. Thymol has been put forward lately in many publications as extremely efficacious against hookworms.

The question of a treatment that will cure bilharzia is rather interesting. Of course, as has been pointed out, that disease is characterized essentially by lesions of the rectum and bladder, and the mere killing of the worm in the portal system, for instance, or in the posterior mesenteric blood vessels does not necessarily mean the cure of the disease. If you can kill the worm, you stop the production of the eggs which are causing the trouble. Another phase of the situation presents itself in this: Whether relief is to be obtained by the removal of the eggs already there. Anything which claims to cure that disease will need careful analysis as to whether we really have what can be termed a cure.

The CHAIRMAN. The Chair would like to add one word. In the Isthmus, the eggs of the Schistosoma munsoni were decidedly common and in only four cases was the parasite found to be pathogenic. I saw one case in San José, Costa Rica, dying with symptoms of proctitis and colitis. I saw three cases in Santo Tomas Hospital, Panama, in the same condition. The syptoms were like those of amebic dysentery, the lesions being unusually low down. At the autopsies that I saw on two cases we found that the rectum was riddled with ulcers, due to the spine of the eggs. No treatment had any effect, as far as anyone could tell, save possibly washing out with ordinary enemata. The point is that all of these cases were from the uplands of Venezuela; none were coast men. Two had come by Chagres, two by Trinidad, and one from Portobelo, but all were men from the mesa. They are the only cases that I can recall. In all there were rectal ulcers. Also autopsy showed ulceration of the lower part of the sigmoid, due to the spines of the eggs.

The CHAIRMAN. The next paper upon the program, "Method of approach in teaching sex ethics to girls and young women," is by Dr. William R. Manning, University of Texas.

A METHOD OF APPROACH IN TEACHING SEX ETHICS TO GIRLS AND YOUNG WOMEN.

By WILLIAM R. MANNING,

University of Texas.

Along with many other educators and with many scientists and social reformers I believe that one of the greatest dangers to present civilization is the perversion of the sex function and sex life. All society, including the State, rests on the home and the home depends on the sex relation. Owing principally to the sex ignorance of women the home is threatened from two directions. The social evil and commercialized vice are withdrawing from home life a considerable percentage of girls and young

women who are by nature "fittest to survive" if considered from the sexual standpoint. The dangerous limitation upon, or entire avoidance of, childbearing is preventing the increase, if it does not actually cause the decrease, of the element of the population that is "fittest to survive" when considered from the intellectual, the social, and financial standpoint. Thus, the sex dangers to which women are subject and the avoidance of sex duties by women threatens to result in a "limitation upon the fittest," if not indeed the "elimination of the fittest," even if they should never entirely destroy the home.

I would not suggest to you one evil thought except to warn you against its danger. There is no evil in a full knowledge of the matters which I am going to discuss, provided that knowledge comes from a wholesome source. But much evil of the very worst kind results from ignorance of them, or from partial knowledge imparted with an improper motive. I would not frighten you unnecessarily by telling of one danger that is not real, or by magnifying dangers that are real. Hidden dangers are the greater because they are concealed. It is the covered trap that catches a wary animal. It is the hidden pitfall or entanglement that involves an attacking army in ruin. It is an invisible mine or a submarine boat that blows a ship to destruction.

I do not wish to cause women to despise or fear men. I would have men and women in each other's company more than they are rather than less. But I would have both observe proper safeguards, each understanding fully the sex nature and sex difficulties of the other, and each realizing the dangers to which unwise conduct in either may subject both.

I would have all girls and women marry, if possible, and be intelligent, considerate, and even indulgent wives; and I wish that all wives could and would become mothers. For no other life can entirely satisfy the true end of their creation, or bring to them so much of happiness and contentment.

I believe that a full understanding of the overpowering strength of men's sex impulses will increase the respect and admiration of all true women for all pure men. No woman, not even a wife, dreams of the effort it costs a man or boy to remain entirely pure. He who lives a perfectly clean sex life is a hero of 10,000 battles—of battles which are the harder to fight because they must be fought absolutely alone, with no praise for victory and little if any shame for defeat.

It does no good to denounce all men as villains, or even those who go down to defeat dragging innocent girls or women with them. It is not enough to declare that many men do win the fight and stay clean, and that all could, if they would live up to the best that is possible for them. More good will be accomplished in teaching them self-control by acknowledging frankly that more men fail in the battle for purity than win, and that the struggle is so great that even the strongest and best remain pure only through valiant and ceaseless effort.

In spite of denunciations and moralizing and theorizing it is hardly likely that man's sex nature will ever be materially changed or the strength of his passions diminished. Incidental proof is afforded by authentic writings, both sacred and secular, that there has been no general material change in the sex nature or sex habits of man during the past 4,000 years. Since there is little if any hope of changing his nature, the only hope is to change his habits by strengthening his self-control and by removing as far as possible all influences which stimulate the normally quiescent and controllable instinct into the all but irresistible whirlwind of passion.

In the meantime the men of the present must be lived with as they are; and the sooner girls and women understand the reason for and the nature of men's sex responses the sooner will they be able to conduct themselves so as to avoid the consequent dangers. Girls and women should be willing to make whatever effort and even sacrifice may be necessary to do this, because these dangers involve not only themselves but also their male associates, their weaker unprotected sisters, their own future home life, and all society.

In giving these very plain talks I have in mind three distinct purposes.

The first and the chief is to promote the safety of girls, and of women, both unmarried and married, by pointing out the dangers to which they are necessarily exposed because of the sex nature and sex problems of men, and by showing how they unconsciously increase these dangers and how they can consciously diminish them.

My second purpose is to increase the happiness and forestall the mental anguish of future wives (and incidentally of their husbands as well) by having the young women of the present understand before marriage the reason and the apparent necessity in nature's economy for the almost overmastering strength and the perpetual presence, but perfect propriety and harmlessness when rightly used, of the sex impulse in men. By this means I hope to do something toward removing what I believe to be one of the most fertile causes of domestic discord and divorce.

My third purpose is to make it easier for men, whether married or unmarried, to live up to the single standard of virtue, thus doing something to limit the spread of the social evil and consequent social diseases, which together are threatening the very existence of the home, and through it of all society, including the State. I propose to do this by showing to girls and women the influence which unwise conduct or improper clothing has on the sex impulses and sex life of the men and boys with whom they come into contact and by appealing to them to do all they can to remove these influences.

I shall endeavor to make these talks perfectly simple by avoiding all technical and abstruse language. I shall also avoid all obscene expressions used by unthinking or vicious men and boys in their all too common conversation among themselves concerning sex matters. But I shall be perfectly plain and shall neither conceal nor omit any facts which I consider necessary for a full understanding of men's sex nature and sex problems and of the reasons for the almost uncontrollable character of their passions. In doing this I shall probably say things for which most men would criticize me severely; but that is because in the case of most men these things recall experiences and sensations which they wish had never come to them and which they would like to forget. It has been my experience and the experience of other men who have dealt with these subjects that women listen to wholesome instruction on them with much less perturbation and much less shamefacedness than men, because most women have not had experiences of which they should be ashamed; and their calmer sex nature is such that they do not experience anything of the thrilling sensations that come to men when they read or listen to such discussions.

Because prevalent social conventions and imperfect ideals of chivalric conduct protect girls and women of the so-called respectable classes from the immediate consequences of the passions which they unconsciously arouse in the men and boys with whom they associate, they think no harm is done, or more probably most of them think nothing at all about it.

In their ignorance they do not realize, and, when informed, they are reluctant to believe, that their unwise conduct, their insufficient or improper clothing, and their undue familiarity have much to do with driving many of these same men and boys to satisfy the passions that they have aroused by seducing girls of a supposedly lower class, who are not protected by these distorted chivalric ideals and false social distinctions, or by visiting the houses of prostitution that are continually recruited from these unfortunate victims of this vicious social system.

For too many of the respectable girls and women their respite from suffering is but a brief one. In marriage many of these same men bring back to them from their fallen sisters the terrible social diseases to cause them lives of suffering, to fill operating rooms with supposedly innocent victims, and to render homes childless or, what is far worse, bring to them imbecile or defective children. These diseases are spoken of by women of the underworld as wedding presents which they send to brides.

It is almost inconceivable how married women, who, if they have normal husbands, know the effect on their husbands of close bodily contact or the exposure of any considerable portions of their bodies, will still expose so much of their bodies to the gaze of other men, and invite, permit, and even urge improper familiarity from other men, and encourage their daughters to do the same.

The only possible way to account for or excuse such conduct on the part of clean wives and mothers is to think that they believe their own husbands abnormal and other men not subject to the same almost uncontrollable passions.

If a husband ventures to criticize his wife's clothing or conduct he is likely to get nothing for his pains but derision or an indignant stormy protest, and possibly a scornful reminder that to the impure all things are impure. Unfortunately many husbands are led themselves to fear that they may be abnormal; and nearly all of the rest, finding criticism worse than useless, give up their attempt to correct what they know is dangerous and accept what they consider inevitable.

More disastrously still, many husbands who would by choice lead clean, proper lives accept the challenge of their wives and indulge in the same improper familiarities with other women, not only of their own social set but of the underworld, also, with the inevitable results. The deluded wife merely exults in thinking that she has won her point and had her way. The husband does not tell her the fearful cost of her victory until some gossip or some too bold act on his part rouses her suspicion and she charges him with unfaithfulness, or until she finds that he has brought to her one of the dreadful diseases to which he is continually exposed.

Even if they were sharing in the profits of organized vice, many popular and reputable but socially ambitious women could hardly do more to stimulate the business than they are now doing.

Girls and young women have long been told in a dogmatic way and in general terms that they ought not to do or permit this thing or another thing which is asserted to be dangerous without the reason being given. Different prophets of evil who utter these warnings disagree concerning almost every one of the things which girls are warned against. This conflicting advice has led many girls to feel that all such warnings are but expressions of the foolish fears of old fogies, and they have defied all advice and abandoned all restraint.

I believe it will be far better for girls and women to be told frankly why certain actions in them necessarily stimulate certain very pleasurable, very alluring, very powerful, and therefore very dangerous impulses in boys and men. With this knowledge I believe they can safely be left to choose intelligently whether they wish to incur the inevitable perils to themselves, to their gentlemen friends, to their unprotected sisters, and to all society. I believe that knowledge will be a more effective shield than ignorance to protect the innocence and purity of our girls and young women.

The old notion that complete silence should be observed concerning sexual matters, that even fathers and mothers should never mention them to their sons and daughters, is now condemned by most enlightened people. It is feared, however, that few parents yet have the courage or the skill to live up to their convictions.

It is certain that few adults of the present generation, and few of the young people now approaching manhood and womanhood, have ever had any proper instruction. But scientific investigations have proved that practically all boys before they reach adolescence even have acquired from older boys a large amount of improper knowledge concerning sex. Usually little else enters into the conversation of adolescent boys when in groups unattended by girls or women or grown men. And too frequently, it must be said to their shame, men not only do not restrain such talk among boys but themselves start and lead it. And among men this obscene talk is all too common. But most young women still come to womanhood in almost complete ignorance of the mysteries of sex. Serious students are agreed that this unfor-

tunate combination of ignorance on the part of girls and young women and vicious knowledge on the part of boys and men is the fertile culture in which the social evil germinates and flourishes and from which commercialized vice derives its supply and support.

It is almost unbelievable that girls should for so long have been kept in such complete ignorance of those matters which contain so much of present peril for them and so vitally affect their whole future welfare. Because of this ignorance thousands fall victims every year to dangers which they could easily have avoided if they had known of their existence. The only serious explanation ever given for this conspiracy of all society against its girls is that it is improper for their pure minds to be soiled with thoughts of impurity.

Every father, while he knows that many girls are led astray, hopes and believes that his daughter many be fortunate enough to remain in innocent ignorance. And the chances are in his favor, since fortunately an overwhelming majority do escape. But each of the thousands who do go down every year is somebody's daughter and might be anybody's.

If a city council should pass an ordinance declaring that henceforth all children should hold their hands over their eyes and their thumbs in their ears while crossing the principal business street, it would be thought very strange. If, when the reason for such an absurd regulation was demanded, they should say that they believed it improper for children to be frightened by knowing the many dangers to which they were exposed, and that few would be killed anyway, since nearly all motormen, chauffeurs, and drivers would try to keep from running them down, that council would be considered better fitted for an insane asylum than for a city hall. But such an ordinance would be no more absurd than the unwritten social law that hides from nearly all girls the vitally important knowledge concerning matters of sex.

It is my desire to uncover your eyes and unstop your ears that you may see and hear and know and escape the sex dangers that you are likely to encounter.

If there were in this city a huge recreation park where each evening thousands of young people, and you among them, were strolling in happy, careless, and apparently innocent freedom; if now and then one girl mysteriously disappeared through a concealed trapdoor never to reappear or be mentioned in respectable society; and if I knew where the trapdoor was and could tell you how to avoid it, would you want me to refrain from telling you, even if the door had an unpleasant name and it would be painful for you to know what became of those who had disappeared through it? Do you think your parents would neglect to tell you if they knew, or would object to my telling you? Hitherto most of them have neglected, although they do know, and probably many would object if they knew that I was going to try to tell you.

Such a recreation place does exist in this city and every other; and the concealed trapdoor frequently opens to receive its victim and closes forever behind her. I am going to try to explain why the door is so treacherous, and to show the many insidious approaches along which it is so easy and seems so harmless to start; and I shall endeavor also to explain why the keeper of the door seems so pleasant when he meets you at the beginning of any of these approaches, but is so utterly heartless when he drags his victim through.

The name of the park is social pleasure. The hidden trapdoor is man's passion. The keeper of the door is man himself. The beginnings of the many approaches are collectively known as sex attraction, or, more familiarly and politely, feminine charm in women and gallantry in men. No one wishes to or can escape or eliminate these beginnings. But if traveled far the approaches lead by imperceptible degrees to the all but irresistible sex stimulation which too frequently ends only beyond the trapdoor from which the man may and does return but the girl almost never.

Parents in the home, teachers in the public schools, preachers in the churches, and teachers in the Sunday schools, all give much time and thought and energy to the

moral training of boys and young men, of girls and young women. All other moral dangers, both great and small, both near and remote, are fully and frankly explained, and the young are told why they should and how they can avoid them. But when anything is encountered in reading or spoken in conversation concerning any sex danger or any sex fact it is passed over in shamefaced silence or condemned as indecent. Yet every normal boy or young man is continually confronted with many most serious sex problems, fraught with the worst sort of moral and physical dangers not only for himself but for the girls and young women with whom he associates.

For girls and young women especially, no other dangers are so serious as sex dangers, and no other offenses are so fatal as sex offenses. Almost any other offense, even though oft repeated, may be forgiven and lived down. A single sex mistake in a girl may and often does hopelessly condemn her to a life of social ostracism, of shame, and of suffering; to a death of despair; and to an eternity the character of which God only in His wisdom can know or in His mercy determine.

I do not think the time has yet come, or ever will come, when these matters should be considered proper for general conversation in company composed of men and women or boys and girls. I certainly think that they should never enter into the conversation of one man and one woman alone (unless they be husband and wife), even though one should be a physician. I doubt very seriously whether it is entirely wise for them to be discussed before mixed audiences from the lecture platform, the stage, the pulpit, or even the teacher's desk. Such instruction is far better than no instruction. But when it is given before segregated audiences by careful and prayerful teachers the dangers are eliminated and the effects are far better. I am so firmly convinced that one boy and one girl or one man and one woman alone ought never to discuss them that I do not want any girl to come alone to ask me questions concerning them. If girls will come to me in groups of two or more I will endeavor to answer any questions; or if anyone for any reason prefers she may come to my home and we will discuss them in the presence of my wife, who is as vitally interested in these matters as I am.

Dr. Morrow, of Philadelphia, a prominent worker in the effort to prevent social vice, in addressing the New Jersey Federation of Women's Clubs, said:

> For centuries past the sex problem has been surrounded with an atmosphere of prudery, unnaturalness, and false modesty. Our traditions and teachings have made of the system of generation a system of shame. The reproductive function, to which the life of the human race is intrusted, has been degraded from its high purpose to purely selfish sensual ends, and we are accustomed to look only at its vicious aspects.
>
> The sex problem has now begun to emerge from the fog of asceticism and prudery which has so long enveloped it and to take its place among the subjects deemed most worthy of serious study. Viewed rightly, the subject of sex, the ever-recurring miracle of generation and birth, is, to use the words of the Rev. Canon Lyttleton, "full of nobleness, purity, and health." There can be no greater satire on creative wisdom than to assume that the function which most nearly assimilates man to his Maker by cooperating in the divine mission of the creation of life is, in any proper sense, shameful or unclean."

To strengthen his position, he quoted from a letter of President Eliot, saying:

> Society must be relieved by sound instruction of the horrible doctrine that the begetting and bearing of children are in the slightest degree sinful or foul processes. That doctrine lies at the root of the feeling of shame in connection with these processes and of the desire for secrecy. The plain fact is that there is nothing on earth so sacred and propitious as the bringing of another normal child into the world in marriage. There is nothing staining or defiling about it, and therefore there is no need for shame or secrecy, but only for pride and joy. This doctrine should be part of the instruction given to all young people.

Later in his address Dr. Morrow declared:

> The most modest, refined, the most womanly of women are not offended by plainness of speech. * * * The explanation of the more open-mindedness of women

to this knowledge is that sex, maternity, and children constitute a larger and more important part of woman's existence and questions relating to such important facts of her life seem natural and proper. Apart from considerations of sentiment women have a right to a knowledge of the facts which so vitally concern their own and their children's health.

The American Society for the Prevention of Social Diseases, in a pamphlet addressed to teachers, declared:

The need of popular instruction in the physiology and hygiene of sex has in recent years become recognized as imperative by many earnest physicians and citizens. The reasons are of a nature that specially requires instruction of the young between the ages of 10 and 20—i. e., when the great majority are in school and college. The ideal is for all parents to give it. Since this is impossible of realization at present, the duty falls chiefly upon physicians and teachers.

Another pamphlet issued by the same society, in discussing the problem for teachers, says:

Sex is the most important fact of life—the central fact as regards the existence and the relations of human society. * * * So far as we can apprehend nature's purpose in the scheme of the universe, the chief end of man and woman is not simply to live, but to transmit life, and from this point of view all other functions of the body exist and need to be conserved to permit of the accomplishment of the creative function. In order to assure the perpetuation of life, nature has implanted in all animals the sexual instinct which incites to the performance of this function; man alone is endowed with reason for its guidance and will for its regulation.

Still another pamphlet, on the relations of social diseases to marriage, says:

Evil conditions, like many crimes, flourish best in the dark. In this atmosphere of ignorance, in disguise and darkness, wearing the protective mantle of secrecy and shame and silence, with absolute exemption from all sanitary recognition or control, these diseases infect the social body, unseen and unnoticed. In view of the dangers which menace the public health and the interests of the family and society from venereal diseases, it is time to break down these barriers of concealment and silence behind which these diseases propagate and flourish, to dissipate the dense ignorance of the public by turning on the purifying light of knowledge, to do away with the mystery and secrecy which have always surrounded them, and to put aside that ridiculous prudery which regards all knowledge of sexual matters as profane.

Dr. Winfield S. Hall, in an address on the teaching of social ethics, said:

The only rational cure for present social conditions is to be found in education. Wise laws justly and firmly administered will help. Public institutions for reclaiming the fallen will also help. These two measures last named alleviate in a superficial way only. What we must seek to accomplish is to remove the cause so that these ills will not exist and therefore not need alleviation. In the social evil, as well as the drink evil, it is necessary that the education—the rational prophylaxis of the evil—be begun in youth. It is very much easier to keep a young life straight than it is to make it straight once it has become bent and distorted. * * * A very small proportion of the present generation of parents possess either the requisite information or the necessary inclination to give this instruction.

There must be a transitional period, during which educators, social workers, and all the constructive forces of society work together to produce a generation of parents who will possess both the information and the inclination. That means that we must go into the schools and teach the great truths of life to the children and youth. * * * The education of the youth in this transitional period should begin in colleges and universities. It may be said in passing that a considerable number of our institutions of higher learning have already made a good start in this teaching. We may look forward with assurance to a time in the near future when all these institutions will recognize their obligation in this direction and will have this instruction given systematically.

In the introduction to his Sex Education Series, Dr. Hall says:

There is need for instruction by religious teachers, since the will and the conscience must be appealed to if right habits are to be formed.

Dr. Robert N. Wilson, in his Education of the Young in Sex Hygiene, discussing the girl's needs, says:

It is the common statement of married women consulting with their physicians that before marriage they knew practically nothing regarding the need of instruction with respect to their own or their life partner's physical body. No one prepared them for unnecessary blunders and dangers before they entered into that richest in happiness and peril of all life's ways. On the score of indelicacy and difficulty of approach, and because of a modesty as false, transparent, and fatal as the affection of Judas for Christ, thousands of young wives have been brought already sexless from disease to the operating table, and thousands more have there been rendered sterile. * * * If the girl of the twentieth century has a single need it is for a simple, sane understanding of her physical self, of her greatest physical object in living, and the means of its fulfillment.

The American Federation for Sex Hygiene, in a committee report on sex education, says:

The common reluctance even of educated people in the past to tolerate discussion of this subject, outside of medical circles, must give way, and is rapidly giving way, to a nobler and purer sentiment, which will recognize that whatever is fundamental and vital to health and morals in the individual and the community is a proper subject for serious thought and discreet discussion.

In order to reach its conclusions, this committee formulated a dozen or more propositions setting forth means and methods of giving sex instruction of all kinds adapted to all ages and classes. These propositions were submitted for approval or disapproval to a large number of representative educators in public schools, colleges, and universities throughout the United States. Every proposition was approved by from 75 to 100 per cent of the hundred or more replies. Of the remainder, few disapproved, most merely expressing doubts. This is indicative of the wonderful and wholesome change of sentiment that is taking place among the educated classes.

Jane Addams in her book, A New Conscience and an Ancient Evil, says:

This first direct step toward an adequate educational approach to this subject has been surprisingly difficult owing to the self-consciousness of grown-up people; for while the children receive the teaching quite simply, their parents often take alarm. * * * A year ago the Bishop of London gathered together a number of influential people and laid before them his convictions that the root of the social evil lay in the so-called "parental modesty," and that in the quickening of the parental conscience lay the hope.

Further on Miss Addams says:

Expert educational opinion is practically agreed that for older children the instruction should not be confined to biology and hygiene, but may come quite naturally in history and literature, which record and portray the havoc wrought by the sexual instinct when uncontrolled, and also show that, when directed and spiritualized, it has become an inspiration to the loftiest devotions and sacrifices. The youth thus taught sees this primal instinct not only as an essential to the continuance of the race, but also, when it is transmuted to the highest ends, as a fundamental factor in social progress. The entire subject is broadened out in his mind as he learns that his own struggle is a common experience. * * * It has been said that the child growing up in the midst of civilization receives from its parents and teachers something of the accumulated experience of the world on all other subjects save upon that of sex. On this one subject alone each generation learns little from its predecessors.

In closing her chapter on moral education and legal protection, Miss Addams says:

Only the protection of all children from the menacing temptations which their youth is unable to withstand will prevent some of them from falling victims to the white-slave traffic; only when moral education is made effective and universal will there be hope for the actual abolition of commercialized vice.

If more expert testimony were necessary or could be found to prove that wholesome instruction in sexual matters is woefully needed, can be given with perfect propriety, and is being given with excellent results.

When murder or some other serious crime has been committed and the criminal has escaped without being observed by anyone and can not be easily found, the police or detectives always raise the question, To whose profit could it have been that this crime should be committed? This clew usually fixes suspicion on some one, and frequently results in the detection of the criminal.

Who profits from this conspiracy of silence concerning sex knowledge, in which nearly all the rest of society joins against its girls and unmarried women?

Certainly the girls and unmarried women get no profit from it. The most that can be said is that a large majority of them fortunately suffer no ill from it so long as they remain unmarried. But no one knows which of them may at any time become one of the small minority who are the first and most unfortunate victims of it, and to whom it brings far worse than death, for it means a life of infamy to end in a death of despair.

Neither do married women profit from it. The knowledge of sexual matters is inevitable to them. When, as usual, they are uninstructed beforehand, it sometimes comes even to those who marry the cleanest and kindest of men with such a shock of dismay, disgust, and fear that it disrupts the marriage at once and ends the dream of happiness. In other cases the wife even of such a man spends the early weeks or months or possibly years in untold agony, thinking she is wedded to a man who is brutal and unlike others. She could have been saved this by knowing in advance that all men are essentially alike, if they are normal, in possessing this powerful instinct, and by being taught that there is nothing shameful, unholy, or injurious in the proper sex relation of husband and wife. More especially the thousands of wives who each year are married to men who have acquired the physical and moral diseases inseparable from social vice (which lives principally on the sex ignorance of girls and unmarried women) certainly get anything but profit from it.

Neither do pure men, either married or unmarried, profit from this conspiracy of silence. The immodest clothing and improper conduct of so many women due to their ignorance of the influence these have on men's sex impulses make much harder than it need be the struggle in which clean men are always engaged to remain pure in thought as well as act.

Those who profit from sex ignorance in girls and women are impure men, who wish to prey upon them, and the army of human harpies, both men and women, who share in the spoils of commercialized vice. Should parents and educators still continue to be, as nearly all have hitherto been through their silence, accessories to this crime?

What I am attempting is a study of sex ethics rather than of sex anatomy or physiology, or even of sex hygiene. It is therefore not my purpose to discuss the structure or uses or care of the sex organs, either male or female, or to study the subject of reproduction in general, although I consider these very important and perfectly proper subjects for discussion or study before classes or audiences composed of women and girls alone or men and boys alone. Furthermore, I would have men and boys know all there is to be known, not only concerning the male sex organs and functions, but the female also; and I would have all women thoroughly instructed not only concerning their own, but those of men as well. In no other way can there be a full and sympathetic understanding by each of the sex problems, difficulties, and dangers of the other. Without such full and sympathetic understanding it is hardly possible for safe and proper relations to be maintained between them.

The traditional and customary habit of thinking of and referring to these portions of our bodies as the secret organs is not only absurd but vicious. It is part and parcel of the age-old and fatal conspiracy of silence concerning sex. I hope the time may come when these will be thought of and spoken of no longer as the secret but as the sacred organs. This would help to inspire a much to be desired reverential respect for them that should lead to their proper care and their preservation and reservation for holy uses.

Fortunately this information concerning the structure, the uses and the care of the sex organs, and concerning reproduction already exists in many books. For a simple and readable and scholarly study of the most important facts concerning the female organs and female share in the reproductive processes, I know of nothing better than Dr. Mary G. Hood's book, "For Girls and the Mothers of Girls," published by the Bobbs-Merrill Co. A similar though somewhat technical but still readable study of the male organs and male share is Dr. Winfield S. Hall's "Reproduction and Sexual Hygiene." His more recent "Sex Education Series" presents much of the same information in simpler form in several small books adapted to various ages. I wish that every girl and woman, and every man and boy as well, would read and re-read with care both of the first two books, or some of the many other books that deal with the same subjects. Dr. Hall's latest and best book, called "Sexual Knowledge," published by The International Bible House, gives full instruction concerning both male and female sex organs and processes, in easily comprehensible language. Dr. I. D. Steinhardt's "Ten Sex Talks to Girls," recently published, is valuable, simple, and wholesome. He also has a companion book on "Ten Sex Talks to Boys."

I shall not attempt to study the character or the prevalence of the terrible diseases that result from the social evil. It is sufficiently startling, and should cause every unmarried woman to be exceedingly cautious, for me to say that the consensus of opinion among students of these subjects and among practicing physicians indicates, in a way that makes it practically impossible to doubt the truth of their statements, that considerably more than half of all men either are or have been infected with one or more of these diseases. In cities the percentage is much higher. In some cases, of course, infection is without illicit relations.

I will dwell long enough to say for your comfort and protection that there is a practical and proper and almost certainly effective way to exercise this caution. It is for every prospective bride (through the medium of her parent or guardian or physician) to require from the man she is to marry certificates of at least three medical examinations declaring that at all three examinations he was free from any of these or other communicable diseases. The physician should be chosen each time not by the man but by the woman or those who speak for her. The times of the examinations should not be selected by him, but by the woman's representatives, and should be unknown to him until a few days before each is to be made. There should be at least one year between the first and the last, and marriage should follow shortly. No clean man will resent or object to the requirement. If one did resent it, that in itself would be strong presumptive evidence of his fear that he could not give a clean bill of health. It would also be proper, and strengthen the evident justice of her cause, for the prospective bride's parent or guardian to give, as a matter of course (not merely to offer), to her prospective husband similar certificates of her freedom from communicable disease. At least one such certificate for each is required by law in some States. It would be far better if the other two were also required, or voluntarily given as just described. This would have the further salutary effect of making hasty marriage impossible.

A multitude of books and pamphlets are available for the study of these social diseases and their relation to health, to marriage, and to society in general. Perhaps the most easily available and effective are the numerous and inexpensive pamphlets issued by the Society of Sanitary and Moral Prophylaxis. Dr. Robert N. Wilson's "Education in Sex Hygiene" is one of the best general studies of reproduction and the social evil, though not the most happily organized from a literary or logical standpoint.

I will do hardly more than to mention the widespread white-slave traffic, the organized means of recruiting for the deplorable system of commercialized vice, which makes it unsafe for any girl or young woman, unmarried or married, to trust herself in the company of any man who is not an acquaintance of at least several weeks or months' standing and of irreproachable character.

"A New Conscience and an Ancient Evil," by Jane Addams

science and an Ancient Evil," already quoted from, is a dramatic and convincing presentation of the extent, the danger, and the methods of this nefarious business. The other books and pamphlets just mentioned study this also.

My discussions will be confined to an effort to give an adequate appreciation of the all but uncontrollable strength of men's sex impulses when under the influence of sex stimulation; to give a reasonable explanation of the almost perpetual presence and easy susceptibility to outside stimulation of their desire for sex union; to show what actions and conditions in women stimulate this desire; and to show women and girls how they can avoid causing this stimulation without depriving themselves or their gentlemen friends or relatives of any legitimate pleasures that come from the proper companionship of the sexes.

Many men who conscientiously oppose the giving of sex instruction to women and others who do not oppose all instruction but think it should not be given so fully or frankly as I am giving it, fear that a knowledge of so seductive a danger will lead some to seek it who might through ignorance escape. Think for a moment. If there were lying in an out-of-the-way corner of this room a small package which you had frequently passed near without touching or paying any attention to, and if I should know and tell you that it contained dynamite which would explode with fatal results to yourself and probably to others if you should strike it or handle it carelessly, would you deliberately go and kick it? Certainly not, if you believed what I said. If there were on this table a glass containing what appeared to be drinking water, but what I knew to be a colorless, odorless, and tasteless but deadly poison, would you be more likely to kill yourself by drinking it after I told you its real nature, or before? Are the young and middle aged people of the present drinking more intoxicating liquor than they would otherwise have done because teachers of physiology and hygiene in the schools for the past two generations have been teaching the evil effects of alcohol? No; it is this very instruction, and that imparted in other ways, that seems to have sounded the death knell of the liquor traffic. And this has come about in spite of the fact that this instruction has not endeavored to conceal the pleasure and exhilarating stimulation which result from moderate drinking, but has dwelt on the certain ultimate evil from even moderate drinking and the danger that moderate drinking will lead to excessive drinking with its shame and disgrace and its moral and physical and financial ruin.

If, then, in order that you may realize how powerful and seductive the dangers are to which women are subjected because of the sex passion in men, I explain to you the almost delirious pleasure which practically all men and possibly a few women experience when under the influence of extreme sexual excitement, is that going to make you more likely to incur these dangers than if you remained in ignorance of them? I believe it will not, any more than a knowledge of the pleasures of intoxication or of opium eating is going to make you a drunkard or an opium fiend.

It is exactly in this almost insatiable delirious pleasure that the strength and persistence of the masculine passion lies; it is the almost uncontrollable strength of that passion that makes it so dangerous; and it is women's ignorance of its universality and strength which leads them unintentionally and unconsciously to stimulate it.

The sex instinct is for the life of the race what hunger is for the life of the individual. Intense "gnawing" hunger is caused by violent spasmodic contractions of the muscular walls of the stomach. Nerves in the stomach convey to the brain the sensations caused by these movements, and a craving for food results. The sex organs are supplied with very numerous and very sensitive nerves. As the continually accumulating reproductive secretions of the male organs cause pressure, their walls periodically and involuntarily become turgid and spasmodically expand and contract. The nerves convey this agitation to the brain and a craving for sex gratification results, whether the boy or man is awake or asleep. This craving is far more insistent than the craving for food, and the pleasure accompanying its satisfaction is immeasurably more intense. Just as hunger grows more intense in the presence of appetizing food,

so this sex longing becomes more intense when stimulated by conditions to be explained.

In men who persist in living continent lives, that is, resolutely resist the powerful temptation to satisfy their longing in any improper way, this "sex hunger" operates as a powerful force impelling them to marriage, which institution has been ordained by God and man for the legitimate satisfaction of this longing and for rearing the children which normally result from it. It is thus seen that this instinct, which is so dangerously insistent, is necessary and, if properly controlled, beneficent.

If any woman is to be entirely safe she must understand the existence and the strength of this instinct, avoid giving occasions for its stimulation, and keep from falling into the power of men of uncertain character or impure habits. Woman's physical strength is useless as a protection; for man, always the stronger, seems to possess almost superhuman strength when under the influence of sex stimulation.

It is in order that you may understand these facts and conduct yourselves accordingly that I am giving you these perfectly frank explanations of the serious sex problems of men. Proper precaution will enable you to avoid almost every danger.

If you will examine with care a fully and freshly opened peach blossom you will see just above and within the circle of five pink petals a mass of tiny stems each having its top enlarged and covered with what seems to be tiny particles of yellow dust, which, if you shake the flower, flies off in a miniature cloud or which clings to your nose or your finger if it touches them. In the middle of the bunch of little yellow-crowned stems you will see a single one slightly larger and considerably longer, which also has its end slightly enlarged, but very different from the others, and covered with a slightly sticky substance. At the bottom of this central stem you will find a little bulb-like enlargement which, if the blossom had remained on the tree and no mishap had befallen it, would have developed into a peach.

These are the sex organs of the peach. The single central stem with its tiny enlargement at the top and its larger bulb at the bottom are the female organs. The smaller yellow-topped stems are the male organs. All other flowers have essentially these same organs, though they may differ greatly in form, in relative location, and relative numbers in different flowers. In some plants the female organs are on different twigs or different boughs from the male, and in some the two are on separate plants or trees.

I probably do not need to inform you that in the beginning God not only created man, male and female, and ordained that each should be a helpmate to the other, but all other living things, both animal and vegetable, except a few of the very lowest forms of life, were also created male and female. And, barring the few relatively unimportant exceptions, without the union of the male and female elements of any given species there can be no new life produced.

Let us turn again to the peach blossom and notice that there is only one female stem. This is called the pistil. The enlargement at the top is the stigma, and that at the bottom the ovary. If you will count the male stems, or stamens, as they are called, you will find that there are 20, 25, or 30 if the flowers are normal and none of the stamens have fallen. Each little enlargement, or anther, as it is called, on top of the stamen contains so many dust particles, called collectively the pollen, that it is almost impossible to count them. There are probably several thousands of them. for a conservative estimate let us say there are a thousand to each. Multiplying this by the number of anthers would give at least 20,000 pollen grains to each flower. Each grain contains a male germ cell and is capable of fertilizing one female germ cell and starting the new life.

In the single ovary at the bottom of the single pistil is just one female germ cell. If this be fertilized by one of the pollen particles it will develop into a peach if it subsequently meets with no mishap. If the seed of the peach, the essential portion

so far as the reproductive process is concerned, be planted it will come up and grow to be a new peach tree.

The fact that I want to impress on your minds concerning the sex process in the peach is that of the 20,000 or more male germ cells only one is needed or can be used. All the rest must go to waste. Certainly in the peach nature is prodigal of the male element, but very careful to make sure that the female shall not lack fertilization.

In many other plants, perhaps most plants, the ovary, instead of containing only one female germ cell and developing into one seed, contains many female germ cells and develops many seeds, as the apple and most berries among fruits, or peas, beans, melons, and most vegetables. In these cases as many pollen particles or male germs as there are seeds must find their way into the ovary, each coming into contact with and fertilizing its own female germ. Even in such cases, however, there are scores, probably hundreds, and possibly thousands, of male cells for each female cell.

The reason for this prodigality of the male element in plant reproduction is probably partly due to the fact that there are only a few days, possibly only a few hours, in the life of the individual flower when the organs are in such a condition that the fertilizing process can occur. If during those few hours or days the male germ fails to find its way through the pistil to the female germ in the ovary, the pistil withers and drops, the unfertilized female germ ceases to grow, and the entire ovary, which would normally have developed into the fruit, being robbed of the purpose for which it existed, also atrophies and drops from the tree.

To prevent this calamity, or reduce its occurrence to a minimum, nature provides hundreds or thousands of male germs to make sure that one of them will perform its mission. She seems not only prodigal of the male germ, but careless of its fate. The lifetime after maturity of the individual male cell is only a few hours or a few days. unless it finds new life in union with the female.

This brevity of life of the unused male germ is common to animals and to man, as well as to flowers. The prodigal profusion in the supply of male germs is also common to them. And the careless waste of the unused germs also exists. More will be said a little later concerning these facts in their relations to animals and to man.

The means by which the pollen from the anther is conveyed to and unites with the ovule in the ovary is the sex process of the flower, or fertilization. I have said that without this there can be no new plant life. The way this is accomplished is very interesting and wonderful. It is possible that the pollen from one flower by merely falling may drop on the stigma of another, or it may be carried by the wind or water from one to the other. But nature has provided a surer means. In most familiar flowers the transfer is effected chiefly, and in some entirely, by insects. Each insect is wholly unconscious of the important service it is performing, being only intent on accomplishing its own selfish ends—that is, satisfying its appetite for food, or for enjoying the sweet odors or gay colors of the flower—purely sensual pleasures, Those features which so please us about the flower—the beautiful color, and the delicate odor—are provided by nature merely to attract the insects to the nectarlike liquid at the base of the pistil, which constitutes their principal food.

By various ingenious devices nature has, in nearly all flowers, made it practically impossible for the pollen from the anthers of any individual flower to reach the stigma of that flower. This is doubtless for the same reason that the stock raiser brings his male animals from other flocks or herds, and that near relatives among human beings are forbidden to marry.

To accomplish this purpose in the peach and many other flowers the pistil is considerably longer than the stamens and the stigma is thus far above the anthers. "While the bee feeds from the honey, hidden at the base of the pistil, its legs and body become dusted with pollen from the anthers. It flies to another flower, still seeking honey, but it also carries the pollen, which is brushed against the pistil of the second flower."

Dr. Hood in her book, "For Girls and the Mothers of Girls," already mentioned and just quoted from, describing this process, especially for the lily, says further:

As the pollen dust is blown by the wind or brought by the insect, it is caught by the sticky fluid upon the stigma. The sticky substance furnishes just the food which the pollen cell finds necessary for its growth, and very shortly it begins to grow and to send down a fine tube through the pistil to reach the ovary. When, after two or three days, the tube is ready, the [sex] nucleus, which is the essential part of the pollen or male cell, escapes into the tube and travels down to meet the ovule, or female cell. When it reaches the bottom of the tube, the end opens, the two cells come together, the ovule absorbs the nucleus, and immediately the changes begin which end in the formation of a seed.

The sex process in animals and man is remarkably analogous to this—that is, through the tube of the female sex organs is inserted the tube from the male organs, and through the latter the male germs pass to find the female germ. In animals and man the sex organs, instead of being created anew for each act of union, as in plants, and immediately disappearing, remain as permanent parts of the entirely separate male and female bodies. The most important difference, however, is in the forces which bring the male and the female germs together.

The flower has neither consciousness nor volition; hence in it sex union must be effected by outside forces. Neither is the insect conscious of the service it renders the flower in effecting the union, any more than the wind is conscious when it renders the service. The insect's act is both voluntary and conscious; but it wills only to satisfy its own appetite, and knows only that it is being satisfied. In fishes and frogs and most other water animals, where fertilization and hatching occur wholly apart from the body of the parent, there seems only little more consciousness or volition in effecting the union than in plants. But in the higher forms of animal life and in man, where the fertilized ovum must spend a period of weeks or months in the body of the female before its expulsion or birth, the union of the germs must occur within the female body and can not be left to chance or be accomplished by forces independent of both parents, as in flowers.

Sex instinct in the higher forms of life takes the place of the color and odor and nectar in the flowers. In most animals both the male and female sex instincts appear to be entirely dormant except when there is in the female's body an ovum in the proper stage for fertilization. When this condition exists, certain actions or sounds or odors always make known the fact. The instinct of the male always responds instantly. In the absence of any influence to keep them apart union always occurs, and normally fertilization follows. During the several months from the time fertilization occurs until some time after the birth of the young, although the two may be continually in close proximity, neither seems conscious of the sex instinct.

If, however, the male animal should at any time, after a few minutes had intervened, come into contact with another female of the same species that was ready for union his instinct would again respond. Hence one male domestic animal is sufficient for scores of females. While the sex process in animals is thus both conscious and voluntary, the individual animal wills only to satisfy the desire of the moment and is conscious of nothing but its satisfaction. So far as being willing to perform, or conscious of performing, a necessary part in reproducing its kind, the service is probably little if any more conscious or voluntary than that of the insect for the flower.

The supply of the male germs in the sex process of animals is almost, if not quite, as prodigal as in flowers. Instead of the single germ or very few needed, thousands pass from the body of the male to that of the female at a single act of union. In addition to this prodigality, the male, among domestic animals at least, is always ready, though his service is needed by an individual female only once or twice a year.

This fact is of great economic value. Since a single male animal or fowl is all that is needed for a large herd or flock, and since the number of males and females is approximately equal, the surplus males among many domestic and some wild animals,

after the few are reserved, can be and are used for food, in case they are edible. In the case of horses and some others, which are not good for food, the males are preserved and used for draft animals. But it is necessary for them to be unsexed, since they are otherwise almost unmanageable, so irresistable is the instinct when stimulated by coming near a receptive female of the same species. Even in many wild animals most of the males are eliminated so far as their service in reproduction is concerned. In fighting for possession of the receptive females the weaker males are killed or driven away by a few of the strongest. In a few species of animals and many of birds there is a pairing-off during the mating season, which gives to practically all males an equal share in reproduction.

Because it is so difficult to control the sex instinct when stimulated, the male horses that are reserved for breeding purposes are seldom seen on the street or the road or in the field, but are shut away in the rear part of livery stables or confined within high strong fences. When taken out skillful horsemen must keep them under constant control by bridle and whip. A bull, when forcibly restrained under such circumstances, although tame and manageable at other times, often becomes so infuriated that he attacks and kills his master.

The fierceness of the sexual passion in males, when under the influence of stimulation, is not confined to animals. It is every whit as strong in men; but the power of self-control is greater, and in that minority of men who remain pure is always effective. Unfortunately, however, the power of self-control in most men is far from being as strong as it should be and is sure to break down sometimes if temptation is strong. In some men self-control is almost wholly lacking at all times. There are certain physical conditions, of which the most serious is intoxication, which deprive even the strongest men of the power to control this instinct.

Even when every other condition is most favorable for exercising this self-control, continued close proximity of a girl or woman, and her apparently yielding familiarity (especially if these occur when considerable portions of her body which should be clothed are exposed) may, and too often does, entirely break down the strongest control. This is why such dreadful crimes can happen, even among those of supposedly irreproachable character, as are frequently reported in the daily press.

When this stage is reached in man there is no strong fence or halter or whip or ring in the nose to control him. Law attempts to cast some safeguards around women and apply some restraint for men, but the law is of very little value for protecting the individual girl from the consequences of the fatal mistake. It affords a little protection for society in general by punishing the worst offenders when their offenses have become the most flagrant. Man's reason and his knowledge of the cost to his victim is a restraint in some cases. Social conventions and notions of decency restrain a few. But in too many cases all of these fail in the presence of a powerful stimulus. The only safe way is to avoid stimulation.

There is one important difference between the sex instinct in man and in male animals and, unfortunately, this increases the danger to women. It was stated above that in most male animals the sex instinct appears to be entirely dormant except in the presence of a female of the same species that is ready for and desirous of union. But in the absence of any stimulation from girls or women, and even in the entire absence of all women, all normal men and boys at some times and some men and boys at nearly all times are conscious of a powerful sex instinct that impels them to seek means for its gratification. This feeling is stimulated by seeing pictures of nude or partially nude women, or women in immodest attitudes or clothing, or even by seeing pictures of a man and a woman in each other's embrace, such as unfortunately have in recent years become all too common on the covers and the pages of what are considered the best magazines. Imagining any of these or a multitude of other sensual facts or pictures has much the same effect. Talking of any such things, or obscene conversation concerning any sexual matters, which has already been said to be dis-

tressingly and even disgracefully common among men and boys, also strengthens this ever present dangerous desire.

Instead of saying that these things cause this desire in men it would probably be more accurate to say that the everpresent powerful instinct is what causes men and boys to engage in obscene conversation, to think lewd thoughts, and to enjoy sensual pictures. But it is certainly true that such pictures, such thoughts, and such conversation strengthen the instinct and render self-control more difficult. Therefore they should be avoided as far as possible.

That the control of this instinct is not entirely subject to the will even in the absence of any or all of these or other stimulants is evident from the fact that during sleep this instinct is often present and causes the mind to conjure up sensual dreams. The dreams usually pass leaving no effect other than the memory. But in normal boys older than 14, and normal men who do not have frequent sex union, there occurs during sleep about once, twice, or three times each month a discharge from the sex organs of the fluid which they are continually secreting, accompanied by much the same sensations as sex union. This usually occurs in connection with the dream, and the sleeper usually awakes at the moment of completion. These nocturnal emissions, sometimes referred to as visits from dream wives, are often, in clean boys and men, the source of great mental disquietude, and not infrequently of nervous, and sometimes physical, injury, since few realize or are properly informed that they are perfectly normal and are experienced by practically all. They resemble the regular monthly discharge from the organs of girls and women in both their periodicity, which is approximately though never entirely regular in men, and in the mental anguish they frequently occasion because proper information concerning them is not imparted at the proper time. Quack doctors and venders of so-called remedies prey upon these fears in boys and sometimes in men, leading them to think that this perfectly natural function is a loss of vitality or virility or an evidence of approaching depletion of strength.

When regular sex relations are formed, whether in wedlock or out, these night manifestations cease. A feeling of comfort and well-being takes the place of uneasiness and discomfort. The disposition is likely to become more cheerful, and the general health may even show marked improvement. Under these circumstances it is not strange that so many men hold to the popular but mistaken notion that frequent sex union is necessary in order to preserve virility and health, and on this ground justify themselves for visiting fallen women until they find it convenient to marry. But the risk, almost amounting to a certainty, of acquiring disease is a fearful price to pay for the comfort and temporary feeling of well-being that they enjoy. The occasional visits from dream wives described above seem to be the means which nature has kindly provided for relief to the boy or unmarried man until legitimate and safe relations can be established by marriage. These nocturnal emissions are entirely adequate so far as preserving health or virility is concerned. They may even be entirely absent in many cases, and no other means of relieving the desire may be practiced, and still no damage be done to health or virility.

In mentioning these serious sex problems which the boy or unmarried man has to contend with if he resolutely refuses to engage in illicit relations, it is proper to mention the fact that many boys discover for themselves, and many others are taught by companions, unnatural methods of producing at will the discharge of the fertilizing fluid, with its accompanying feeling of physical pleasure, without the assistance of any woman. The undesirableness and certain injury of this habit, properly called masturbation, is sufficiently indicated by saying that the names by which it is usually known, when the conversation is not of an obscene character, are "self-abuse" and "secret vice." It usually accompanies, and sometimes apparently causes, imbecility and insanity. It may be practiced for a considerable time without the boy being conscious of its wrongfulness or realizing its injuriousness. But when he learns its

true character and endeavors to break the habit he realises its overmastering strength and in his apparently vain struggle against it his reason may, and at times does, entirely break down. As long as it is practiced the night discharges are likely to be absent. But it is nearly sure to be practiced much more frequently than the normal nocturnal emissions, as the power of self-control is gradually undermined; and the continually repeated nervous shock would be nearly sure sooner or later to destroy health, and probably virility, and possibly reason, even though no effort were made to break the habit.

The existence in men and boys of this powerful instinct, the almost continual desire for gratification, and the almost insuperable difficulty of resisting the desire even in the absence of any stimulation, show why so many men respond so easily and quickly to even a slight stimulation and entirely lose the little self-control that remains. A knowledge of these facts should cause all girls and women studiously to avoid doing anything to stimulate this instinct in the men with whom they associate, and to be very careful to keep from exposing themselves to attacks from unknown men whose power of self-control may already be gone and who may be lying in wait to victimize the first woman that comes within their power.

It is not easy to see why nature should have found it necessary to make this instinct in men so overpowering and so nearly perpetually present. It does seem that it would have been far better if it could have been as it is in the male animal—that is, entirely dormant except in the presence of a woman in whose body a female germ was ready for fertilization, and who desired sex union.

Some think, and possibly properly, that the real cause is to be found in the fact that women's reason has led them to realize so vividly the inconvenience and discomfort of child bearing that they refuse to reveal their desire when they have any, and conceal the fact when prepared for conception. Women having practiced this deceit for so many centuries the sex instinct in many, possibly most, is almost wholly lacking even when conception could take place. The individual woman seems almost unconscious of having more sexual desire at one time than at any other. In many not only is there an absence of desire practically always but sex union with their husbands is distasteful or actually repellant at nearly all times, and sometimes even when they are willing, or actually desire, to bear children. When to this absence of desire through perversion of instinct there is added the stress of economic conditions or the desire in both parents to limit the number of children that a few may be given better advantages than would be possible for many, the danger of race suicide becomes imminent, at least of that portion of the race that is best fitted through intellectual attainments to survive. If sex instinct in men were as weak as in women the danger of race suicide would be far more imminent. According to this theory, as the power of women's sex instinct has declined that of men has become stronger, more continually active, and more uncompromisingly persistent, in order that nature's purpose may not be thwarted.

Whatever is the correct theory to account for it, or whether it can be or need be accounted for, the fact is that men's instinct is almost continuously present, is exceedingly powerful, and in some almost uncontrollable. Any girl may and many girls do fall victims to it because in their ignorance of these facts they unintentionally and unconsciously stimulate it.

The CHAIRMAN. The next paper, "Antirabic vaccination in Habana, with statistics compared with those of other nations," by Dr. Juan Santos Fernández, of Habana, Cuba, will be read by Dr. Guiteras.

ANTIRABIC VACCINATION IN HABANA WITH STATISTICS COMPARED WITH THOSE OF OTHER NATIONS.

By JUAN SANTOS FERNÁNDEZ.

Director of the Laboratory of Antirabic Vaccination of Habana.

Antirabic vaccination in Habana was first used in 1887 (1) immediately after Pasteur discovered it in Paris, Cuba being one of the first countries to adopt it and the first in America to make use of it. Since that time in spite of the great difficulties that the Island of Cuba has encountered, Habana and the country at large have always had at their disposal this powerful remedy to combat certain death, for that was what happened to the person who was bitten by a rabid dog.

Until 1873 it was hard to ascertain the number of victims of rabies in Cuba, but in that year there appeared in the death statistics of this city, the first deaths by hydrophobia. We have to agree, says Dr. Acosta who was in charge of the antirabic treatment from 1887 until his premature death in 1913, that probably there were many cases of rabies that were not mentioned, on account of its being an almost unknown disease and not of easy diagnosis. The first statistics of antirabic vaccination in Habana (2) which were published by Dr. Acosta comprises the first 10 years and he said at that time: Hydrophobia has been known in Cuba since 1838 according to the facts that we were able to obtain and in that epoch 22 people were the victims of the disease. Later on, during General Tacon's administration, the man in charge of the keys to the doors of the city was torn to pieces by mad dogs at the outskirts of the town. This abundance of dogs can only be compared to conditions in Constantinople (3) where there are more than 80,000 dogs, which on account of religious prejudices are not molested by the police. In spite of that, rabies are rare among these mongrels, probably because of the lack of communication with dogs of other countries.

Since the foundation of the laboratory in 1887 it has been known that rabies was frequent in Habana and that its victims necessarily had to be numerous. The number of patients who came to the laboratory in order to be injected during the first 10 years of its establishment was 1,721, according to the facts gathered by Dr. Acosta. Of these, 995 were adults and 721 children, and from them only 543 adults and 313 children, or 856 in all, were innoculated with the vaccine. Adults bitten by animals positive of rabies numbered 134; children, 179. Adults bitten by animals suspected of being rabid numbered 134; children, 366. In reference to the place of the wound: On the head, 12; body, 5; and extremities 163. From this total there have ocurred 14 deaths, giving a percentage of 1.63. Of these 9 were adults and 5 children, a percentage of 1.65 for the adults and 1.58 for the children.

The mortality is low if one considers the fact that during the same period there occurred the deaths of 40 persons who did not come to the laboratory to be treated. If we use the above proportion, we would see that those 40 deaths would correspond to over 5,000 persons who were bitten without having come to the institution, a thing that could not have been so.

Dr. Acosta believed that mortality was greatly reduced after the treatment, while the mortality rate of those not treated reached 50 per cent. Dr. Acosta concludes by stating that at that time mortality by rabies was reduced in France to 0.75 per cent; in St. Petersburg, to 2.65 per cent; in Odessa, to 1.41 per cent; and in Milan to 0.65 per cent.

We shall now describe the statistics of antirabic vaccination in Habana from 1887 to 1915, during the 28 years of its existence in Cuba. In these statistics are included those of Dr. Acosta and one can observe the diminution in the mortality to which he called attention. Our own statistics are as follows:

	Patients treated.	Deaths.	Mortality.		Patients treated.	Deaths.	Mortality.
			Per cent.				*Per cent.*
1887	86	1	1.15	1902	13	.....	.....
1888	95	.....	.....	1903	10	.....	.....
1889	259	3	1.15	1904	22	.....	.....
1890	154	5	3.24	1905	20	.....	.....
1891	115	3	2.60	1906	12	.....	.....
1892	82	.....	.....	1907	8	.....	.....
1893	45	2	4.44	1908	15	.....	.....
1894	72	.....	.....	1909	395	2	0.50
1895	137	.....	.....	1910	343	2	.58
1896	68	.....	.....	1911	408	2	.48
1897	80	.....	.....	1912	162	.....	.....
1898	155	4	2.58	1913	187	1	.53
1899	44	.....	.....	1914	220	2	.90
1900	68	.....	.....	1915 [1]	293	1	.36
1901	10	.....	.....				

[1] During 1915 there occurred three deaths, but only one died after the treatment. Case I came to the laboratory after the disease was established, dying on the second day of the treatment. Case II was bitten on the face by a rabid dog, and after having three day's treatment did not continue, dying a month afterward. Only Case III received the full course of treatment and died two months after that. Thus we feel we are right in including only that one case in the mortality records.

From April, 1887, to this time there have been 4,438 cases in the laboratory, of which 3,360 received treatment and 1,075 were not treated because there was no need for it. In 1,015 there was bacteriological comprobation of rabies in the brains of the dead animals, and of the others, 1,557 were bitten by unknown animals, while the rest, 791, were bitten by animals that had been killed immediately or soon after the occurrence. The existence of the disease in the animals was proved in 354 cases in this laboratory, 118 at the National Laboratory, and 543 according to the reports of various veterinary surgeons.

Since the establishment of the institution 65 persons died from hydrophobia who had not received treatment and 28 died after the treatment, which gives a percentage of mortality of 0.85 per cent, this per cent being very near those of the New York Board of Health and the Pasteur Institute.

Pasteur Institute statistics.

	Patients inoculated.	Deaths.	Per cent.		Patients inoculated.	Deaths.	Per cent.
1886	2,671	25	0.94	1899	1,614	4	0.25
1887	1,770	14	.79	1900	1,420	4	.28
1888	1,622	9	.55	1901	1,321	5	.38
1889	1,830	7	.38	1902	1,006	2	.18
1890	1,540	5	.32	1903	628	2	.32
1891	1,559	4	.25	1904	755	3	.39
1892	1,790	4	.22	1905	721	3	.41
1893	1,648	6	.36	1906	772	1	.13
1894	1,387	7	.50	1907	786	3	.38
1895	1,520	5	.33	1908	524	1	.19
1896	1,308	4	.30	1909	467	1	.25
1897	1,521	6	.39	1910	401	.....	.....
1898	1,465	3	.20				

We were given the statistics for three years of the New York Board of Health which will give a complete understanding of the work done there. During that time there have been inoculated 2,050 persons who were bitten by rabid or suspected animals, and 10 cases of rabies have occurred, 7 of which were of rapid incubation and 3 cases that resulted in death after treatment.

The laboratory of vaccination is under the direction of the New York Department of Health and in one of its departments is Dr. Anna Wessels Williams, who is in charge of the diagnosis of the brains of rabid animals. Her investigations caused her to believe

what is now certain: Negri's bodies are positive, if present, but if not present, one can not say that there are no rabies.

The extraction of the medulla as practiced in New York is similar to our method. The spinal canal is not uncovered, but the cord is pushed with a wire one-half centimeter in diameter with a cotton swab on the end, that is introduced in the anterior part of the canal while the cord is grasped with forceps, and after dried is kept in flasks ad hoc, from which they are taken for the preparation of the virus.

The CHAIRMAN. Our secretary has informed me that the following papers will be read by title and spread upon the record:

Ensayo sobre profilaxia de la sífilis y la blenorragia, by Joaquín Travieso.

Morbosidad y mortalidad infecto-contagiosa en El Uruguay, by Alfredo Vidal y Fuentes.

ENSAYO SOBRE PROFILAXIA DE LA SÍFILIS Y LA BLENORRAGIA.

Por JOAQUIN TRAVIESO,

Médico Asistente de la Facultad de Medicina de Montevideo, Montevideo, Uruguay.

El problema de la profilaxia de la sífilis y demás afecciones venéreas está, sin duda de ninguna especie, aún por resolver.

Tan racionales y eficaces han sido las medidas tomadas en materia de profilaxis para todas las otras plagas que aquejan a la humanidad, como incompleto e imperfecto es lo que hasta ahora se ha hecho en la higiene sexual; todo el camino está por andar y si bien hay países que han obtenido resultados no despreciables, ellos son mínimos, sin ningun valor: se pierden ante la inmensidad de los que ya están enfermos y de los que se enferman a diario.

La profilaxia de la sífilis es una de las cuestiones más serias, más graves, más terribles y más difíciles de resolver, entre las múltiples que se plantean al higienista de nuestros días.

No quiero, no debo disertar sobre porcentajes ni hacer estadística: ya hay muchas; bastan y sobran. No puedo ni debo decir tampoco en este trabajo, que es la sífilis, ni cuáles son sus consecuencias, porque todos los médicos lo sabemos; eso sí, debo, sintéticamente, como hombre, como médico y como especialista, manifestar lo que entiendo por profilaxia de sífilis y demás afecciones venéreas, y cuáles son los medios, que de acuerdo con mi criterio, pueden llevar a la solución del problema.

Ante todo, es necesario que los poderes públicos de todas las naciones del mundo legislen sobre sífilis y blenorragia: la forma, que no podría ser única para todos los pueblos, sería adaptada a cada medio, teniendo como fundamento la educación sexual de las generaciones presentes y, sobre todo, de las futuras.

Hay necesidad de educar a los que son ya hombres; hay que enseñar, que decir, que hacer ver, en todas las esferas sociales, lo que es la sífilis, lo que es la blenorragia, como se pueden evitar, como se pueden adquirir, cuáles son sus peligros inmediatos o lejanos; y a los que son ya víctimas, decirles sus responsabilidades y hacerles comprender lo que significa tener una sífilis o una blenorragia, ya sea por ellos mismos, ya por los demás. Los poderes públicos, secundarán a los médicos en esta obra, pero a éstos corresponde iniciarla puesto que son los únicos capaces de poder abordar el problema de un modo eficaz. En todas las cosas que afectan a la colectividad humana toda entera, las responsabilidades son a menudo compartidas entre muchos, y es así que si hay actos, y a veces ideas que merezcan ser castigados, hay también casos,

y éste es uno de ellos, en que la falta de valor (ya que la ausencia de convicciones de podría argüirse) para ejecutar un acto o defender una idea, son mucho más, cien mil veces más justiciables de castigo y de sanción; se delinque obrando y hablando, pero también se delinque no haciendo y callando. Y en esta materia son responsables aquellos que callen y que no hagan, los médicos y quienes deban secundarlos, los poderes públicos. Para educar al pueblo, a la juventud de mañana, es indispensable que en los albores de la sexualidad humana intervenza el médico, él mismo, y jamás intermediarios que serán las más de las veces incompetentes.

Cuando la primera curiosidad sexual del niño se diseñe en su espíritu, el médico debe tomar la orientación y la dirección de esa importante faz de la vida. Debe ilustrarlo, enseñarlo, satisfacerlo y, al mismo tiempo, dirigirlo por la senda de la verdad y de lo útil, y no por el error y por el engaño como, amargamente tenemos que reconocerlo todos, se hace hoy en día. En las escuelas, cursos especiales deben ser dictados por el médico mismo a los niños de cierta edad, para ambos sexos, separadamente. Es indudable que no se debe pretender el establecimiento de un límite fijo en la edad del niño, para empezar su educación sexual; dicho límite debe variar no solamente para cada nación, sino hasta para cada individuo; y por tanto, no sería difícil en los colegios poder establecer una especie de selección entre aquellos que a juicio del médico y del maestro fueren capaces de retirar fruto de esa enseñanza. En términos generales podría limitarse entre 13 y 16 años la edad más apropiada para inculcar al niño las primeras nociones sobre cuestiones sexuales. Y esa educación sexual, tal vez difícil de resolver en sus detalles, deberá hacerse en una forma clara, sumaria, pero lo más completa posible, quedando sobrentendido que hay que adaptarla a la edad de los auditores. Y en todas las instituciones a donde acuda el niño debe de proporcionarsele esa educación especial tan necesaria en la lucha por la vida, como la del manejo de las armas en la guerra. Pero, si así, los hombres de mañana conocerán esas cosas, nuestros contemporáneos las ignoran, y las ignoran de la manera más completa; pero esto no sería nada si no existiera, como corolario de ese estado de cosas, una serie de prejuicios e ideas falsas que son tan terriblemente malos como la ignorancia misma; esos prejuicios han llegado a todos los medios sociales; esas ideas erróneas se han infiltrado, se han arraigado como se arraiga todo lo malo; tenemos que ponerles fin; tenemos que destruirlos, y al sustituirlos por la verdad habremos cumplido uno de los deberes más sagrados de nuestro apostolado profesional.

Tenemos que ir a las escuelas, a los talleres, a las fábricas, a donde están las familias, al campo, al ejército y a la marina, por todos lados; tanto al hogar del pobre como al del potentado, porque todos necesitan igualmente de nuestra enseñanza. Al niño se le debe enseñar la verdad a fin de que mañana no sea dominado por las historias erróneas que a veces le forjan sus mismos progenitores, ocultándoles todo lo real, lo útil y lo práctico, sino preparándolo para no caer fácilmente en cualquier ocasión, la cual algunas veces pueda hacerlo su víctima en la primera circunstancia.

El pudor no está reñido con la verdad ni con la higiene o la conservación de la especie y su mejoramiento; el pudor está en pugna con los degenerados y los débiles, porque ellos lo ofenden y lo mancillan; estos seres son a menudo víctimas de una sífilis, que sus antepasados, gentes de un pudor sin mácula, les legaron.

Es mucho más fácil perderse en el caos, en el desierto inmenso de la vida, siendo un ignorante, un hombre de prejuicios, que siendo un conocedor en cualquier materia; y si al niño no se le enseña la verdad, él aprenderá la mentira, pagando después su tributo a ella.

Yo no sé pedagogía; como profano en la ciencia de la enseñanza, no podría ni querría sostener con tesis filosóficas más o menos brillantes y acertadas, las opiniones y creencias que profeso en materia de profilaxia. No sé si una vez impregnado de esa difícil ciencia que se llama "pedagogía," y en la más terrible de todas, la filosofía, y si se quiere, en la moral más estricta y absoluta; no sé, repito, si ello haría cambiar mis convicciones y evolucionar mi conciencia en otro sentido; hoy por hoy soy creyente

decidido, un budista de la educación sexual precozmente instaurada en todas partes y en todos los países. La juventud que vendrá tiene derecho a saber, para su salvaguardia personal y para el bien colectiva de ella y los suyos. Hago el cargo formal, severo e inflexible, a esos criterios filosóficos, morales y pedagógicos, que por más hermosos que ellos sean, por más bellas que fueren las concepciones que representan, no valen, no pueden valer seguramente, el aniquilamiento de un hombre, de una familia y tal vez de una generación entera llevado a cabo por la sífilis. Entiendo que debo declarar que si hay derechos que se opongan a la educación sexual de la juventud, yo gritaría que ellos son absurdos. Hay que enseñar a los padres para que ellos enseñen a sus hijos; hay que cambiar sus erróneos conceptos sobre moralidad y decirles bien fuerte que si no nos oyen, serán culpables mañana. Muchos casos podría citar, y lo haré en un libro que preparo en estos momentos, para demostrarles la sinrazón de su conducta y lo torcido de su educación moral en estas cuestiones.

A las masas que viven en las urbes inmensas de las capitales, hay que inculcarles los conocimientos indispensables de higiene sexual; son y serán sus armas eficaces en la lucha contra las enfermedades venéreas. Hay que hacerlo con la palabra, con la imagen y con el ejemplo, y no olvidar tampoco al campesino, cuyos alcances sabemos que no son muy grandes en ningún país del mundo. Habrá que castigar—las leyes se encargarán de ello—a los que conscientemente contaminen a su prójimo, porque una vez conseguido el desideratum de la educación sexual, todos sabrán lo que significa tener una sífilis o una blenorragia, y no podrán alegar ignorancia en esas cosas. Habrá que impedir que se engendren hijos degenerados, exigiendo certificados médicos en forma seria y de una manera general, pues los exámenes serológicos nos permiten, hoy en día, ponernos a cubierto, de una manera casi perfecta, contra las gentes de mala fe. Habrá que exigir una reacción negativa antes del matrimonio y castigar al que desobedezca las leyes, o legislar, haciendo obligatorio el examen médico. Yo conozco varios casos de sujetos en pleno período secundario, que han contraído matrimonio, y uno de ellos a quien amonesté de la manera más severa, ya ha contaminado a su esposa. En casos como éste, habrá que librar al médico de su secreto profesional, y más aún, darle los medios de impedir la consumación de tales hechos. La literatura médica registra casos de médicos que han denunciado a uno de los contrayentes matrimoniales como portador de una sífilis en plena potencia; y yo los justifico, pues entiendo que no puede existir ningún deber profesional que oblique a hacerse cómplice de un acto semejante ni pueda acallar nuestra conciencia de médicos y de hombres.

Y no hay que creer que es solamente en ciertas clases inferiores de la sociedad, donde existen arraigadas ideas funestas sobre sexualidad y enfermedades venéreas es en todos los ambientes, en todas las esferas donde hay tal estado de cosas, y más aún, en todos o casi todos los países es lo mismo; y entre los que hemos tenido la suerte de conocer algunos países que marchan a la cabeza de la civilización del mundo, y de vivir en ellos, no nos faltarían argumentos y casos para probar las afirmaciones que acabamos de hacer: en Europa—y ésto es la expresión más sincera de la verdad—la educación del pueblo a este respecto no es superior ni mucho mejor que la nuestra, y ¿por qué no decirlo de una vez? Es completamente nula; no existe.

La prostitución es indudablemente una de las causas principales de diseminación de la sífilis y la blenorragia, y si bien tanto reglamentaristas como abolicionistas, tienen y hacen valer hermosos argumentos en favor de las ideas que sostienen, así de una parte como de otra, han desaprovechado un tiempo que hubiera sido precioso.

El reglamentarista dice: revísese toda mujer con la frecuencia necesaria, y a la más mínima sospecha reclúyasela en un lugar apropiado, el sifilicornio, y será así imposible que ella pueda contaminar a alguien más. Esto, sin dejar de reconocer que es eminentemente práctico y útil en ciertos medios especiales, falla fundamentalmente, por dos razones: (a) la revisión debiera hacerse a diario, y aunque así fuera, una pequeñísima lesión puede escapar al ojo más avezado; (b) un contacto precedente, si las prescripciones de la higiene son descuidadas, como acontece muy a menudo, puede

contaminar al que siga inmediatamente, y ésto aún estando la mujer sana. Así se explicarán esos casos en que dos sujetos han estado con la misma mujer, con muy poco tiempo de diferencia, el uno contrae una infección venérea, no infectándose el otro: el primero, en general, es el que enferma con más facilidad, pero a menudo sucede que los dos enferman.

La reacción de Wassermann, hecha sistemáticamente a toda prostituta, y un tratamiento llevado hasta obtener la negativa completa de esa sero-reacción no sólo en la sangre, sino en el líquido céfalo raquídeo, constituiría una garantía en extremo eficaz.

Por otra parte, la escuela abolicionista arguye: (*a*) la prostitución reglamentada a base de reclusión obligatoria de las meretrices, no hace más que fomentar la prostitución clandestina y favorecer su diseminación. Y ésto, no hay más remedio que reconocerlo, es perfectamente cierto. En todas las ciudades que he visitado y en algunas de ellas donde he vivido bastante tiempo se observa perfectamente ese hecho: en Paris todos saben lo que es la prostitución en qué forma está reglamentada, y para qué sirve esa reglamentación; en Montevideo, puede decirse que por cada prostituta inscrita hay 10 que no lo están; y es lo mismo en todas partes. En Montevideo he podido comprobar numéricamente la exactitud de lo que digo. La mujer que ha sido recluida una vez, por más dulce que se quiera hacer su encierro, a su salida, si encuentra una casa no inscrita, lo que no es difícil, cambia inmediatamente, o de lo contrario vive en otra forma más peligrosa todavía, trabajando en rendezvous, yendo a los hoteles y casas amuebladas y frecuentando ciertos pequeños círculos de diversión privados y a veces acudiendo a horas especiales a casas de citas donde elude por completo, así como los propietarios de ellas, toda responsabilidad. Los abolicionistas agregan: nadie tiene el derecho de encerrar a una mujer porque esté enferma: pero dado que esta medida fuera de una utilidad de carácter general y positivo, no se podría dejar de argüir que la mujer que comercia con sus órganos genitales, constituye una profesional que puede presentar serios peligros para la colectividad; en tales casos nadie dudará en internarla, pero si bien esa medida no es del todo inútil, está lejos, pero muy lejos de llenar, ni siquiera medianamente, las necesidades de la profilaxia y la higiene severas que en materia de sífilis y blenorragia debieran ser de rigor. La mejor enseñanza la tenemos en nuestro ambiente, en Montevideo, donde la prostitución clandestina constituye una verdadera vergüenza nacional. Pero los reglamentaristas abogan por su causa diciendo que la persecucion tenaz y firme de la prostitución clandestina, solucionaría el problema. Yo me permito decir que el pretender extirparla de cualquier punto es sencillamente una utopia, y más en países como el nuestro, donde ciertas influencias y causas especiales, que no pueden escribirse, lo hacen imposible.

La educación sexual del hombre y de la mujer hecha completa, el establecimiento de dispensarios especiales sin restricciones de ningún género, donde el enfermo pueda conservar el incógnito, donde no tenga el más mínimo desembolso que efectuar, donde se le aconseje y se le dirija; cuando esos dispensarios funcionen en forma conveniente, cuando su abundancia y su situación sean juiciosamente establecidas, darán seguramente hermosos resultados. En Lieja, en Paris y en algunos puntos de Italia, hay establecidos ya dispensarios de esta índole y parece que, sencillamente, sus resultados han sido magníficos.

En síntesis, cuatro proposiciones dignas de atención me permito presentar a la consideración de ese Honorable Congreso, y son las siguientes:

1ª. Educación sexual amplia, completa si es posible, a los niños y a los adultos, hecha por los mismos médicos y llevada a todos los ámbitos y a todas las esferas sociales de cada país, y educación hecha por la palabra, por el libro y por la imagen.

2ª. Legislación sobre sífilis y demás enfermedades venéreas, en una forma adaptada a las necesidades de cada país.

3ª. Establecimiento de dispensarios múltiples, en todas las ciudades, en todos los pueblos, hasta en las pequeñas localidades.

4ª. Abolición, en términos generales, de la prostitución reglamentada, con excepción de ciertos medios, pero debiendo siempre ser considerada como elemento secundario ante las tres proposiciones precedentes.

Esta breve exposición no constituye más que la síntesis de un extenso trabajo que en estos momentos preparo, y en el que estudiaré en detalle la organización y práctica de cada uno de los puntos fundamentales, proponiendo fórmulas generales que serán modificadas de acuerdo con las necesidades de cada medio.

MORBOSIDAD Y MORTALIDAD INFECTO-CONTAGIOSA EN EL URUGUAY.

Por ALFREDO VIDAL Y FUENTES,

Montevideo, Uruguay.

En el decenio 1905–1914 la enfermedad que dió más denuncias en la República, fué la tuberculosis pulmonar y laringea, alcanzando su cifra a 16,423. Ella fué también la que produjo más defunciones (12,630).

Estaas cifras aterradoras han convencido a los poderes públicos y al pueblo del Uruguay, de la necesidad urgente que hay de combatir ese terrible mal, ensanchándose considerablemente el Hospital Fermin Ferreira, destinado a la asistencia de los tuberculosos; coadyuvando al sostenimiento de las ligas contra la tuberculosis, que contribuyen con su acción eficaz a ayudar a los míseros enfermos bacilares y creando numerosos dispensarios donde se asisten los enfermos y se les da al mismo tiempo datos útiles, que contribuyen a la profilaxia de tan terrible mal.

El sarampión da la cifra de la denuncia más alta después de la tuberculosis, 10,000 casos. La mortalidad por esta enfermedad (326) no es alta y sería más baja aún, si no fuera porque en campaña, debido a la escasez de asistencia médica, se producen muchas complicaciones bronco-pulmonares, que son la mayor parte de las veces las causas de esas defunciones.

Viene después la fiebre tifoidea, con una denuncia de 7,751 casos y 2,009 defunciones. En las ciudades del interior y litoral del Uruguay, las obras de saneamiento están proyectadas, pero aun no se han realizado. Esa es la causa del desarrollo de la tifoidea en nuestro país, que tenderá a desaparecer cuando en aquellas ciudades, se beba un agua tan pura como en Montevideo.

No obstante que esta multiplicidad de casos, debiera aprovecharse para la preparación de la vacuna antitífica, pues constituye un hermoso material para ello, el Instituto Nacional de Higiene, no ha podido aun atender el pedido que le hizo el Consejo Nacional de Higiene, de que la preparara en cantidad, para enviarla a los delegados sanitarios departamentales, con el objeto de usarla en la campaña como medio de profilaxia.

La difteria y la escarlatina son las enfermedades más denunciadas después de las anteriores. En nuestro país se usa mucho el suero antidiftérico, preparado por el Instituto Nacional de Higiene, pero se usa con más facilidad en Montevideo, donde la asistencia médica es rápida y por lo mismo eficaz; mientras que en la campaña, cuando la autoridad sanitaria tiene conocimiento de la existencia de un foco de difteria y acude a él para combatirlo, el terrible mal ya ha producido sus efectos destructores, siendo a veces muchos los que han fallecido sin asistencia médica, antes de la llegada del delegado sanitario departamental.

Puede afirmarse que la mortalidad por difteria en el Uruguay, es dos veces mayor en la campaña que en Montevideo, capital de la república.

La viruela produjo violenta epidemia en el año 1910, alcanzando la denuncia a la cifra de 1,838 y la mortalidad a 599. Si se observa el cuadro adjunto, se podrá com-

probar que esos números, alcanzan respectivamente a más de la mitad, de las cifras correspondientes al decenio, en lo que respecta a la viruela.

Esta enorme epidemia tomó su origen en el año anterior y vino a producirse por un error de diagnóstico. Se describió una púrpura hemorrágica en un hospital, cuando en realidad se trataba de una viruela hemorrágica. Cuando se comprendió el error, ya la chispa había determinado el incendio.

Debido a este hecho lamentable, es que desde 1911, aparecen entre los de enfermedades contagiosas en el Uruguay, los casos de púrpura, como puede verse en el cuadro citado.

Junto con esta comunicación va la Ordenanza No. 136, dictada por el Consejo Nacional de Higiene, el 16 de septiembre de 1910, incluyendo a la púrpura hemorrágica entre las enfermedades de declaración obligatoria.

Con esa misma fecha dictó el consejo la Ordenanza No. 135, que también la agregamos a este informe, por la que se establece la declaración obligatoria de los casos sospechosos de viruela.

Se agrega igualmente la circular de 25 de abril de 1911, que dirigió el Consejo Nacional de Higiene a sus delegados sanitarios, relacionada con el aislamiento en los casos de viruela, escarlatina y difteria.

Junto con todas estas disposiciones tendientes a evitar la propagación de la viruela, la Intendencia Municipal en Montevideo y el Consejo Nacional de Higiene en la campaña practicaron en 1910 una intensa vacunación, habiéndose inoculado en la capital 45,000 personas y en el resto de la República unos 60,000.

El Uruguay tenía en ese año 1,500,000 habitantes.

El éxito de estas medidas, bien meditadas por cierto y que fueron aplicadas con toda energía, no se dejó esperar, pues en los años 1912, 1913, 1914 y hasta el 31 de octubre de 1915, no se ha producido ni un solo caso de viruela en la República.

Han llegado a veces vapores de ultramar, con algún enfermo de viruela, pero no se les ha permitido desembarcar en Montevideo, llevándoseles para su asistencia y aislamiento al Lazareto de la Isla de Flores.

Las primeras denuncias de meningitis cerebro-espinal epidémica, aparecen, como puede verse en el cuadro adjunto, en el año 1913. En ese año se dictó la Ordenanza No. 149, que va agregada a este informe.

El tracoma se estableció que era obligatoria su declaración, por la Ordenanza No. 153 del 12 de octubre de 1914, la cual va también agregada más adelante.

Se denunciaron de esa enfermedad 7 casos.

De beri-beri se han denunciado en este decenio 105 enfermos y 4 defunciones.

Esa enfermedad es completamente exótica en nuestro país, siendo todos esos casos importados, no habiéndose observado jamás ningún caso de beri-beri ni entre el personal del Lazareto, donde todos fueron asistidos, ni entre los demás habitantes del país.

La peste bubónica da 63 denuncias y 13 defunciones en el decenio, habiendo habido años como 1905, 1906 y 1910 en que no se produjo ningún caso de esa enfermedad.

La peste siempre nos vino del Paraguay, del Brasil, de la Argentina y alguna vez quizá de la India, de donde se importa la arpillera, en cuyos fardos se han encontrado ratas.

Los casos se han asistido todos en aislamiento, en el Hospital Fermin Ferreira, en pabellones especiales destinados a ese efectos.

El suero Jerssin aplicado al principio casi siempre fué eficaz. Se le prepara en el Instituto Nacional de Higiene.

Los casos denunciados de lepra se asisten en aislamiento la mayor parte de ellos, en una pequeña leprosería que funciona en el Hospital Fermin Ferreira.

La proporción de la mortalidad infecto-contagiosa por cada 1,000 habitantes, da una idea de que el estado sanitario del país ha sido bastante favorable.

Véase el cuadro adjunto donde está indicada esa proporción para la República, para Montevideo y para la campaña.

Morbosidad y mortalidad infecto-contagiosa y proporción de esta última por 1,000 habitantes en la República del Uruguay durante 10 años, 1905–1914.

[Referencias: D=Declarados; F=Fallecidos.]

Diagnósticos.	1905		1906		1907		1908		1909		1910		1911		1912		1913		1914		Total.	
	D.	F.	D.	F.	D.	F.	D.	F.	D.	F.	D.	F.	D.	F.	D.	F.	D.	F.	D.	F.	D.	F.
Sarampión	624	14	2,269	90	944	21	675	39	578	8	1,672	54	923	38	1,096	22	1,083	36	136	4	10,000	326
Escarlatina	522	79	359	25	209	13	216	29	738	147	102	21	299	13	377	6	261	11	264	1	3,347	345
Viruela	444	140	50	9	16	4	73	2	404	106	1,338	599	380	42	.....	.....	.....	.....	.....	.....	3,265	902
Varicela	350	1	152	1	288	.....	131	1	347	.....	497	1	232	.....	221	.....	302	.....	291	1	2,811	5
Púrpura hemorrágica	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	6	2	4	2	5	4	4	4	19	12
Erisipela	.....	.....	5	1	36	8	24	14	59	11	37	10	34	13	27	7	32	10	37	3	291	77
Difteria	307	76	277	40	296	45	332	46	368	46	276	51	357	59	370	47	465	62	534	63	3,582	535
Tifoidea	491	153	1,190	290	961	235	615	167	578	192	537	224	849	192	1,149	243	734	178	647	135	7,751	2,009
Infección puerperal	50	45	43	32	43	55	61	52	48	45	57	58	72	43	93	58	82	57	94	57	643	302
Tos convulsa	154	13	287	48	145	45	47	25	72	32	93	39	352	46	556	57	99	12	210	7	2,015	324
Tuberculosis pulmonar y laríngea	1,332	969	1,428	1,190	1,272	1,172	1,113	1,112	1,119	1,229	1,314	1,234	2,147	1,441	2,191	1,441	2,129	1,329	2,378	1,540	16,423	12,630
Lepra	6	2	14	8	18	1	17	12	8	4	2	8	8	6	9	3	11	5	9	2	102	51
Tracoma	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	7	.....	7	.....
Peste	.....	.....	.....	.....	17	4	23	5	4	1	.....	.....	4	.....	4	1	9	2	2	.....	63	13
Meningitis cerebro-espinal	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	17	15	5	3	22	18
Beri-beri	.....	.....	.....	.....	.....	.....	15	.....	18	1	24	.....	4	.....	10	1	12	.....	22	2	105	4
Tifus exantemático	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....
Totales en la República	4,280	1,492	6,074	1,734	4,245	1,603	3,342	1,504	4,401	1,822	6,449	2,299	5,667	1,895	6,107	1,861	5,241	1,721	4,640	1,822	50,446	17,753
Montevideo	2,731	724	3,967	833	2,450	722	2,028	722	2,977	964	3,822	1,291	2,416	906	2,720	947	2,206	771	1,973	945	27,292	8,825
Campaña	1,549	768	2,107	901	1,795	881	1,314	782	1,424	858	2,627	1,008	3,251	989	3,387	914	3,033	950	2,667	877	23,154	8,928
Mortalidad infecto-contagiosa por 1,000 habitantes en la República		1.44		1.58		1.40		1.42		1.66		2.03		1.60		1.51		1.34		1.38	.....	.....
Mortalidad infecto-contagiosa por 1,000 habitantes en Montevideo		2.42		2.70		2.32		2.31		3.00		3.93		2.67		2.72		2.14		2.59	.....	.....
Mortalidad infecto-contagiosa por 1,000 habitantes en los departamentos de Campaña		1.04		1.16		1.06		1.05		1.10		1.25		1.18		1.04		1.03		.92	.....	.....

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ORDENANZA No. 136.

MONTEVIDEO, SEPTIEMBRE 16 DE 1910.

Considerando: Que durante la actual epidemia de viruela, se han confundido algunos casos de forma hemorrágica con casos de púrpura;

Considerando: Que cada uno de ellos ha dado lugar a repetidos casos de viruela;

Considerando: Que había necesidad de evitar la reproducción de esos hechos que han contribuido a la difusión de esa enfermedad, y también por la importancia que tendría esa medida del punto de vista de la profilaxis;

Por tales consideraciones, el Consejo Nacional de Higiene en uso de sus atribuciones, resuelve:

ARTÍCULO 1º. Declarar de acuerdo con el artículo 1º de la Ordenanza No. 6, incluída la púrpura hemorrágica entre las enfermedades de declaración obligatoria.

Art 2º. Publíquese para conocimiento general.

ALFREDO VIDAL Y FUENTES, *Presidente.*
JOSÉ MARTIRENÉ, *Secretario.*

CONSEJO NACIONAL DE HIGIENE, ORDENANZA No. 135.

MONTEVIDEO, *Septiembre 16 de 1910.*

Considerando: Que en la ordenanza sobre declaración obligatoria de las enermedades contagiosas, de fecha 28 de julio de 1896, no están incluídos los casos sospechosos de viruela;

Considerando: Que la acción preventiva de la autoridad sanitaria debería hacerse sentir tanto en los casos sospechosos como en los confirmados;

Considerando: Que haciéndose obligatoria la declaración de esos casos se podría intervenir con la anticipación necesaria para establecer las medidas de profilaxis;

Considerando: Que por la misma razón que se ha obligado a declarar los casos sospechosos de cólera, fiebre amarilla, peste y difteria, debiera obligarse a declarar los de viruela;

Por tales consideraciones, el Consejo Nacional de Higiene en uso de sus atribuciones, resuelve:

ARTÍCULO 1º. Declarar de acuerdo con lo prescrito en el artículo 1º de la Ordenanza No. 6, incluídos los casos sospechosos de viruela entre los de declaración obligatoria de enfermedades infecto-contagiosas.

ART. 2º. Publíquese para conocimiento general.

ALFREDO VIDAL Y FUENTES, *Presidente.*
JOSÉ MARTIRENÉ, *Secretario.*

CIRCULAR.

Habiendo consultado la inspección departamental de higiene de San José, cuanto tiempo debía mantenerse el aislamiento, tratándose de viruela, escarlatina y difteria, este consejo, después de oir a la inspección de sanidad terrestre, dictó la siguiente resolución:

MONTEVIDEO, *25 de Abril de 1911.*

El consejo en sesión de esta fecha, aprobó el informe precedente, excepto las conclusiones, que se acordó suprimirlas, sustituyéndolas por la siguiente resolución:

1º. Quien debe juzgar de la duración del aislamiento, es el inspector de higiene, cuyo funcionario intervendrá en todos los casos que lo estime necesario.

2º. El aislamiento se levantará para la viruela y para la escarlatina cuando haya terminado el período de escamación, y en la difteria a los 15 días después de iniciada la enfermedad.

3º. Esta resolución tendrá carácter general y se comunicará a las inspecciones departamentales de higiene para su conocimiento y observancia.

Cumplido, archívese.

El criterio que informa la primera conclusión, no es de que siempre deba intervenir el inspector de higiene para levantar el aislamiento, no; lo que se pretende es facultarlo para que pueda ejercer ese contralor en todos los casos que por razones especiales juzgue prematuro el cese del aislamiento, o cuando tenga motivos de otro orden para dudar de si ha llegado o no el momento de dejar sin efecto la expresada medida profiláctica.

Lo que participo a Vd. a sus efectos.

Saluda a Vd. atentamente.

A. VIDAL Y FUENTES, *Presidente.*
P. PRADO, *Secretario.*

ORDENANZA No. 153.

MONTEVIDEO, *12 de Octubre de 1914.*

El Consejo Nacional de Higiene en uso de las atribuciones que le confiere la ley de 31 de octubre de 1895, debidamente autorizado, resuelve:

Artículo 1º Declárase el "Tracoma" entre las enfermedades infecto-contagiosas de declaración obligatoria a que se refiere el artículo 1º de la Ordenanza No. 6 del Consejo Nacional de Higiene, promulgada por el Poder Ejecutivo con fecha 28 de julio de 1896.

ART. 2º. Publíquese para conocimiento general.

A. VIDAL Y FUENTES, *Presidente.*
JOSÉ MAINGINOU, *Secretario.*

ORDENANZA No. 149 DEL CONSEJO NACIONAL DE HIGIENE POR LA QUE SE INCLUYE LA MENINGITIS CEREBRO-ESPINAL EPIDÉMICA ENTRE LAS ENFERMEDADES INFECTO-CONTAGIOSAS DE DECLARACIÓN OBLIGATORIA—23 DE JUNIO DE 1913.

CONSEJO NACIONAL DE HIGIENE.

El Consejo Nacional de Higiene, en uso de las facultades que le confiere la ley de 31 de octubre de 1895 debidamente autorizado, resuelve:

ARTICULO 1°. Incluir la meningitis cerebro-espinal epidémica entre las enfermedades infecto-contagiosa denunciables de conformidad con el artículo 2° de la Ordenanza No. 6 promulgada el 28 de julio de 1896 y del artículo 26 del Reglamento de Sanidad Terrestre.

ART. 2°. La meningitis cerebro-espinal epidémica queda incorporada a las enfermedades mencionadas en el número 1 del artículo 102 del Reglamento de Sanidad Terrestre.

ART. 3°. Publíquese para conocimiento general.

A. VIDAL Y FUENTES, *Presidente.*
José MARTIRENE, *Secretario.*

The CHAIRMAN. I beg to announce that copies of the following printed books have been presented by the authors to the congress through Section VIII:

Reorganización del Servicio Médico-Legal en Chile, by I. Marcial Rivera.

Essai sur les Diptères Vulnérants du Venezuela, by J. M. R. Surcouf and R. Gonzalez-Rincones. A. Maloine, éditeur. Paris, 1912.

Manual de obstetricia, por los doctores Josué A. Beruti y Domingo Iraeta. Las Ciencias, Librería y Casa Editora de A. Guidi Buffarini, Buenos Aires, 1915.

La Núcleo-Proteína Gonocóccica y sus aplicaciones, por los doctores Silvio Dessy y F. L. Grapiolo. "La Semana Médica" Imp. de obras de E. Spinelli, Buenos Aires, 1914.

The CHAIRMAN. The last paper on our program is "A historical résumé of the investigations of yellow fever leading up to the findings of the Reed board," and is by the late Gen. George M. Sternberg, United States Army, paper to be read by Col. Hoff.

A HISTORICAL RÉSUMÉ OF THE INVESTIGATIONS OF YELLOW FEVER LEADING UP TO THE FINDINGS OF THE REED BOARD.

By GEORGE M. STERNBERG,
Surgeon General, United States Army, retired.

[Gen. Sternberg died in Washington, D. C., November 3, 1915, and this paper was read by Col. John Van Hoff, United States Army Medical Corps.]

It is generally recognized that the demonstration that yellow fever is transmitted by mosquitoes of the genus Stegomyia is one of the greatest achievements of modern science; and the credit for this demonstration is justly given to the commission of which Maj. Walter Reed, surgeon, United States Army, was president, which was sent to Habana in 1900, upon the recommendation of the writer, then Surgeon General of the Army.

Dr. Carlos Finlay, of Habana, had long before conceived the idea that the disease under consideration is transmitted by mosquitoes, and full credit should be given him for persistently advocating this theory, although his own experiments failed to furnish

any satisfactory proof that his theory was well founded. Indeed, such proof was wanting in the earlier experiments of the Reed board, and it was not until, as a final experiment, the mosquitoes, after filling themselves with blood from a yellow-fever patient, were kept for 10 or 12 days before allowing them to bite a susceptible individual that success was attained.

In a report published in May, 1901, Maj. Reed says: "We have thus far succeeded in conveying yellow fever to 12 individuals by means of the bites of contaminated mosquitoes." Confirmation of these results was soon after afforded by the experiments of Dr. John Guiteras, and to-day yellow-fever prophylaxis is successfully based upon this epoch-making discovery.

But as to the precise nature of the etiological agent or "germ," we are still uncertain, although in the present state of science we can scarcely fail to believe in a living germ, which multiplies in the blood of infected individuals, but which is so minute that it has not yet been demonstrated by the highest powers of the microscope.

I have no new facts to add to our knowledge of yellow-fever etiology. But it has occurred to me that a brief account of the investigations which led up to the demonstration that yellow fever is transmitted by mosquitoes might be of some interest to the members of the Pan American Scientific Congress. Such an account must begin with the Habana Yellow Fever Commission of 1879.

The wide extent and great mortality of the yellow-fever epidemic of 1878 led to the organization of a United States National Board of Health. And it was evidently expected that one of the most important duties of this board would be to attempt to devise methods for the prevention of similar epidemics.

Among the members of this National Board of Health was Dr. S. M. Bemis, of New Orleans, who no doubt had much to do with the selection of the members of the commission which it was decided should be sent to Habana to study the disease in one of its principal endemic foci. The membership of this commission was as follows: President, Dr. Stanford E. Chaillé, of New Orleans; secretary, Surg. George M. Sternberg, United States Army; Dr. John Guiteras, Marine Hospital Service; and Mr. T. S. Hardee, civil engineer, of New Orleans. Mr. Rudolph Matas, of New Orleans, was appointed clerk to the commission, and Mr. Henry Mancel, a Frenchman living in New Orleans, was engaged as photographer.

In the division of our work it was decided that Dr. Chaillé should make investigations relating to the prevalence of yellow fever in the island of Cuba. This he did in a most comprehensive manner, as is shown by his published report to the National Board of Health. Dr. Guiteras undertook the search for microorganisms and for pathological changes in the tissues of yellow-fever cadavers. This he did *secundem artem*, but his painstaking labors did not throw any new light upon the etiology of the disease.

To me was assigned the examination of the blood, culture experiments, and experiments upon lower animals. It would be tedious to attempt to give details of my numerous experiments and observations, but suffice it to say that I failed to find any microorganisms in the blood of living patients drawn on different days of sickness and did not succeed in producing any symptoms resembling yellow fever in the lower animals subjected to experiment.

I may say that in advance of my visit to Habana I had strong hopes that by modern methods of research the germ of this infectious disease might be found in the blood, and I was prepared to photograph it if found. I was provided with Zeiss one-twelfth and one-eighteenth inch homogeneous oil-immersion objective, and I had received instructions in the art of making photomicrographs from Surg. J. J. Woodward, United States Army, a pioneer and recognized expert in the art, at the Army Medical Museum. Ninety-eight specimens from 41 undoubted cases of yellow fever were carefully studied, with a completely negative result so far as microorganisms were concerned. My photomicrographs were mostly made with a magnifying power of 1,450 diameters, obtained by the use of a Zeiss one-eighteenth inch objective and a Tolles amplifier.

The researches made by me subsequently to the return of the yellow fever commission were embodied in my report on the Etiology and Prevention of Yellow Fever published in 1890. In it I say:

The investigations to which this report relates were made in the city of Habana in the summers of 1888 and 1889; in the city of Decatur, Ala., in the autumn of 1888; and in the laboratories of the Johns Hopkins University, where I have continued my researches during the intervals between my visits to the infected localities, and since my return from Habana, in September, 1889, up to the present date.

My bacteriological studies have been made with material obtained from 43 yellow-fever cadavers; from "black vomit" and feces of patients in various stages of the disease; and, for comparison, from 18 cadavers in which death occurred from some other disease than yellow fever, and from feces of healthy individuals.

After the extended researches in this report I state my conclusions as follows:

The experimental data recorded in this report show that the specific infectious agent in yellow fever has not been demonstrated.

The most approved bacteriological methods fail to demonstrate the constant presence of any particular microorganisms in the blood and tissues of yellow fever cadavers.

The microorganisms which are sometimes obtained in cultures from the blood and tissues are present in comparatively small numbers, and the one most frequently found (Bacterium coli commune) is present in the intestines of healthy individuals, and consequently its occasional presence can not have any etiological import.

A few scattered bacilli are present in the liver and probably in other organs at the moment of death. This is shown by preserving portions of liver, obtained at a recent autopsy, in an antiseptic wrapping.

At the end of 24 to 48 hours the interior of a piece of liver so preserved contains a large number of bacilli of various species, the most abundant being those heretofore mentioned as occasionally found in fresh-liver tissue—viz, Bacterium coli commune and Bacillus cadaveris.

Having failed to demonstrate the presence of a specific "germ" in the blood and tissues, it seemed possible that it is to be found in the alimentary canal, as is the case in cholera. But the extended researches made and recorded in the present report show that the contents of the intestines of yellow-fever cases contain a great variety of bacilli and not a nearly pure culture of a single species, as is the case in recent and typical cases of cholera.

On the other hand nonliquefying bacilli are very abundant. The one most constantly and abundantly present is the Bacterium coli commune of Escherich. This is associated with various other bacilli, some of which are strict anaerobics and some facultative anaerobics.

Among the facultative anaerobics is one (my bacillus X) which has been isolated by the culture method in a considerable number of cases and may have been present in all. This bacillus has not been encountered in the comparative experiments made. It is very pathogenic for rabbits when injected into the cavity of the abdomen. It is possible that this bacillus is concerned in the etiology of yellow fever, but no satisfactory evidence that this is the case has been obtained by experiments on the lower animals, and it has not been found in such numbers as to warrant the inference that it is the veritable infectious agent.

All other microorganisms obtained in pure cultures from yellow-fever cadavers appear to be excluded, either by having been identified with known species, or by having been found in comparative researches made outside of the area of yellow-fever prevalence, or by the fact that they have been found only in small numbers and in a limited number of cases.

It will be seen that I did not positively exclude my bacillus X as a possible etiological factor, but I say that it was not found "in such numbers as to warrant the inference that it is the veritable infectious agent." In 1902 I was appointed Surgeon General of the Army, and my opportunities for personal research work ceased. My published reports had apparently satisfied the profession that the various claims which had been made for the discovery of the specific germ of yellow fever had no substantial foundation. Among these were the claims of Domingos Freire, of Brazil; of Carmona y Valle, of Mexico; of Carlos Finlay,[1] of Habana; and of Paul Gibier, of France.

[1] His "Micrococcus tetragenus febris flavae."

Since my report above referred to was published a new claimant appeared—viz, the Italian bacteriologist, Sanarelli. His researches were made in Brazil, and, singularly enough, he found in the blood of the first case examined by him a bacillus. It was present in large numbers, but this case is unique, for neither Sanarelli nor anyone else has since found it in such abundance. It has been found in small numbers in the blood and tissues of yellow-fever cadavers in a certain number of cases examined. For a time I thought it probable that Sanarelli's bacillus was identical with my bacillus X. But the researches of the Reed board identified it with the bacillus of hog cholera, while my bacillus X appeared to them to belong to the colon group. The bacillus of Sanarelli had a certain amount of standing for a time because two medical officers of the Marine Hospital Service, who had been sent to Habana to study yellow fever, made a report favorable to the claims of Sanarelli. But the researches of Reed, Carroll, and Agramonte [1] have demonstrated conclusively that this bacillus has nothing to do with the etiology of yellow fever.

At the present date Dr. Aristides Agramonte is the only living member of the yellow-fever commission appointed upon my recommendation in 1900. Maj. Walter Reed, surgeon, United States Army, was selected as president of this commission because he was a trained bacteriologist, and at the time of his appointment was in charge of our bacteriological laboratory at the Army Medical Museum. He died in Washington from appendicitis November 23, 1902, aged 51. Since his death various articles published in the newspapers have stated that he died as a result of his yellow-fever investigations. This is a mistake. Dr. Reed was in Washington at the time that Dr. Carroll made upon himself the first successful yellow-fever inoculation and he was not inoculated.

Dr. James Carroll died in Washington March 9, 1907, of myocarditis, which was believed by his physicians to have resulted from the severe attack of yellow fever which he suffered in 1900.

Dr. Jesse W. Lazear, contract surgeon, United States Army, was appointed a member of the commission because he had had special training as a bacteriologist. He died at Camp Columbia, Cuba, of yellow fever on September 25, 1900. His attack was attributed to the bite of a mosquito while he was visiting the wards of a yellow-fever hospital.

The written instructions given by me to this selected board of experts were as follows:

You will naturally give special attention to questions relating to the etiology and prevention of yellow fever. As you are familiar with what has already been done by other bacteriologists in this field of investigation, I do not consider it necessary to give you any suggestions or detailed instructions. But it is evident that the most important question which will occupy your attention is that which relates to the etiology of this disease.

You will also take advantage of such opportunities as may offer for the study of other infectious diseases, and especially of the malarial fevers prevailing in the island of Cuba. An important question in connection with the diseases of tropical and semitropical countries relates to the etiology of febrile attacks of short duration, to which strangers are especially subject. Should you have time, there will be ample opportunity for the study of leprosy in the lepers' hospital in the city of Habana. Attention should also be given to the infectious diseases of the lower animals, in case any such prevail, the etiology of which has not been definitely determined.

In addition to these written instructions I talked freely with Maj. Reed, president of the commission, and gave him my views as to the most promising lines of experiments relating to the etiology of yellow fever.

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[1] Dr. Agramonte worked on this problem during the Santiago campaign in 1898 and afterwards with Reed and Carroll in the bacteriological laboratory of the Army Medical Museum. He was ordered to Habana in December, 1898, with instructions from Gen. Sternberg and power to do all that might be necessary to clear up the problem. In 1899 Drs. Geddings and Wardin submitted a report affirming that Sanarelli's bacillus was present in almost all the cases, while Dr. Agramonte denied that it had such specific character and showed its occurrence in cases not yellow fever. He continued his researches until appointed a member of the commission.

I urged that efforts should be made to ascertain definitely whether the disease can be communicated from man to man by blood inoculations. Evidently if this is the case the blood must contain the living infectious agent upon which the propagation of the disease depends, notwithstanding the fact that all attempts to demonstrate the presence of such a germ in the blood, by means of the microscope and culture methods, had proved unavailing. I had previously demonstrated by repeated experiments that inoculations of yellow-fever blood into lower animals—dogs, rabbits, guinea pigs—give a negative result, but this negative result might well be because these animals were not susceptible to the disease and could not be accepted as showing that the germ of yellow fever was not present in the blood. A single inoculation experiment on man had been made at my request in the city of Vera Cruz, in 1887, by Dr. Daniel Ruiz, who was in charge of the civil hospital in that city. But this experiment was inconclusive for the reason that the patient from whom the blood was obtained was in the eighth day of the disease, and it was quite possible that the specific germ might have been present at an earlier period, and that after a certain number of days the natural resources of the body are sufficient to effect its destruction or in some way to cause its disappearance from the circulation.

I was especially anxious that this experiment should be repeated with the blood taken from a case in the early stages of the disease. I had not been able to make the experiment upon myself, as I was immune, having suffered a severe attack of yellow fever in 1875.

The Reed Commission made this experiment with success after having demonstrated that the disease could be transmitted by mosquitoes which had been kept for 10 or 12 days after biting a yellow-fever patient. It is evident that if the experiment had been made at the outset of the investigation a similar success would have lead inevitably to the conclusion that yellow fever, like malarial fever, is transmitted by an intermediate host, and that this intermediate host is a mosquito.

So far as I am concerned, there is nothing more to be said about yellow-fever etiology, and my excuse for writing this brief paper is to be found in the fact that the present generation of physicians had not appeared upon the stage when Prof. Chaille, Dr. John Guiteras, and myself visited Habana in 1879 for the purpose of studying yellow fever, and probably few of the members of the profession have seen my published report of subsequent investigations made by me.[1]

The CHAIRMAN. You have heard the paper. It is now open for discussion.

Dr. AGRAMONTE. I need hardly say how gratified I am for the opportunity of hearing this paper, prepared by Surg. Gen. Sternberg a short time evidently before his recent death. I am sure that I have never overestimated the great value of his investigations when I have said, as I frequently have, that his work was of the utmost importance; that he blazed the trail that made the walking easier for those who came after him. As I listened to the reading of his paper it seemed to me like an echo of a voice from beyond the grave and like a proof that the lives of great men do not terminate with their earthly existence.

Dr. GUITERAS. I rise, of course, not for discussion, but in memory of this kindly gentleman, Dr. Sternberg.

[1] This historical résumé was prepared a few weeks before the lamented death of Gen. Sternberg and is an important contribution to the history of the momentous period treated of, all of which the writer knew and a large part of which he was.

Dr. KOBER. I will simply state for the information of the section that this paper might not have been presented to the section if Mrs. Sternberg had not noticed in one of the daily papers a remark that was made by Dr. Agramonte that the organism of yellow fever had not yet been discovered. She was reminded, then, that the general had prepared a paper on this subject. She placed the paper in my hands only four days ago—a most opportune moment to place on record an historical résumé of the preliminary work which led up to this brilliant discovery. It is very evident that the paper was prepared with no intention of detracting in the slightest degree from the brilliant achievements of the Reed Yellow Fever Commission, but to recount his own preliminary work, which certainly was of the highest scientific value and has enabled future investigators to begin where he left off. He had done the work, with practically nothing more to be added than absolute experimentation on the human subject. This fact, gentlemen, must go down in history in justice to a man who was as able as he was modest.

The CHAIRMAN. The more I think of the history of the etiology of yellow fever, the more surprised I am that we could not see what Finlay showed us. I can take a little credit to myself that after meeting him I thought his view was, at least, reasonable. In the second year that I was at Habana we found that Las Animas Hospital, where the yellow-fever patients were treated, at least the hospital proper, was practically noninfectible territory. The physician who had been there a whole year without contracting yellow fever, did contract it when he moved into town the next spring. One of the nurses who had nursed in Las Animas the whole summer of 1899, when she went down in the spring of 1900 into Habana contracted yellow fever. It was fair, then, to say that Las Animas was noninfectible territory. I suggested that there be put out in both the lazareto and the main hospital, bottles to get the larvæ of the mosquito, thinking that since these places were uninfectible territory this mosquito was not the factor that carried it, if we found it. I was decidedly disappointed in finding some of these larvæ hatched in the bottles, more in the lazareto than in the hospital. I did not think of finding them in the lazareto because it was fumigated with sulphur every week or so. I suppose the reason that the fever was not conveyed into the hospital, was possibly because the patients were kept until the diagnosis was very certain before they went in. I think a very small percentage went in until they had passed the first four days of their sickness, when we believe their blood is no longer infected with the stegomyia. Again, Dr. Guiteras tells me there were but few larvæ. We found some, however. But Finlay was that close to proving his belief of conveyance by the mosquito.

Sternberg doubtless must have suspected, or must at least have considered the probability of conveyance by an insect host, and yet he could not have readily accepted it. On the 4th of July, 1900, I was dining with Stark, at that time a captain or lieutenant in the Medical Corps of the Army. I was talking to Reed and Chaillé while waiting for dinner. I had been fairly intimate with Lazear before that. The question came up of the mosquito conveyance of yellow fever, and I asked Reed if he had seen the mosquitoes that Lazear had from Finlay, mosquitoes the larvæ of which I myself had carried from Finlay to Lazear. We were speaking of the general conveyance, and Chaillé asked about the conveyance of fomites. I asked if conveyance was by clothing, and Gen. Sternberg stated it was universally admitted that yellow fever was carried by clothing. I think then he must have considered the possibility of insect conveyance, but he had not suspected the mosquito, at any rate, or Reed could scarcely have so quoted him. I told him that the difference between "universally admitted" and proven is very great, that "two years before it was universally admitted that malaria was simply an air-borne disease. It is not so now, and I am one who does not believe it is carried by fomites," and gave him reasons for my thinking so.

I say this to show that I suspect the result was almost as much a surprise to Gen. Sternberg as it was to many others. Lazear was probably the first member of the commission who entertained the idea of the disease being carried by the mosquito. Sometime before Reed came down he said, speaking of some data which had been given him, "This, if true, looks as though it were carried by a living host." I made him a memorandum, showing that there were two other modes of conveyance, which seemed to me also possible.

Col. HOFF. There were two objects sought in reading this paper—one to record that the general had this congress in mind, and the other to bring to the attention of the members of this section the fact that there is probably much in the history of the steps that led up to the final achievement that has been forgotten in the course of events.

Mr Chairman, before a final adjournment of this section I have several resolutions and, with the permission of the section, I should like to introduce them.

The CHAIRMAN. There is no reason why you should not introduce them. I am very sure the section will agree to waiving the method we have used because there is now no committee.

Col. HOFF (reading);

Resolved, That the secretary be requested to send a set of reprints of the valuable papers read before Section VIII of the Second Pan American Scientific Congress to the

following libraries: Library Surgeon General's Office, United States Army, Washington, D. C., Library Harvard Medical School; Boston Medical Library, Boston, Mass.; Library, Academy of Medicine, New York City; Library College of Physicians, Philadelphia; Library University of Pennsylvania; Library Johns Hopkins Medical School.

Dr. HINSDALE. I have no doubt that these papers could be sent without a resolution on application of these particular bodies, but I think perhaps it is just as well to make a record of it.

Seconded and approved.

Col. HOFF. Another resolution:

Resolved, That the Section on Public Health and Medical Science indorses the House of Representatives bill 528 to discontinue the use of the Fahrenheit thermometer scale in Government publications.

Seconded.

Dr. HOFFMAN. May I speak to that resolution? It seems to me that it is too radical a resolution to be passed without serious consideration. If the Fahrenheit scale is to be discontinued it would seem at least advisable that for a time it should be continued in addition to the others.

The CHAIRMAN. I will read from the bill. (Read.)

Dr. HOFFMAN. That meets the objection.

Motion carried.

Col. HOFF. A further resolution, sir:

Resolved, That the thanks of the section are due and that they be extended to Maj. E. R. Whitmore, our most efficient secretary, for the admirable way in which he has performed the arduous and exacting duties of his office and which has resulted in a most successful meeting of our section on public health and medical science.

The CHAIRMAN. I move that the vote on that resolution be taken standing.

The members of the section rose.

Col. HOFF:

Resolved, That the thanks of the section are due to the Latin American members of the section, and especially to Drs. Guiteras and Agramonte, for their assistance in promoting the efficient conduct of the section.

The CHAIRMAN. All in favor will rise.

The members of the section rose.

Col. HOFF. I move that we adjourn.

The CHAIRMAN. It is moved that we adjourn sine die.

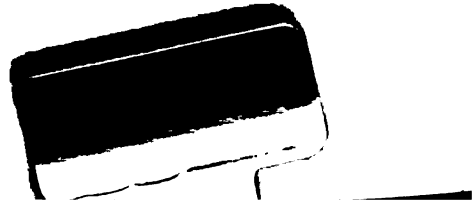
Adjournment sine die of Section VIII.

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